



CASE REPORT

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## A rare case of type IV hypersensitivity: Prilocaine allergy

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### Abstract

Allergic reactions caused by local anesthetics are quite rare and these reactions often manifest as Type I (immediate-type) hypersensitivity; however, Type IV (delayed-type) hypersensitivity reactions also hold clinical significance. Type IV reactions are generally T-lymphocyte mediated and symptoms appear hours or days after antigen exposure. In this case report, a rare Type IV hypersensitivity reaction to prilocaine, an amide-type local anesthetic, is described. The patient presented to our center due to the delayed-onset skin lesions that developed after previous surgical procedures and was evaluated through comprehensive allergy testing. A positive delayed-type reaction to prilocaine was observed in the intradermal and patch tests; however, no reaction was detected in the provocation test performed with mepivacaine. This highlights the importance of careful selection of local anesthetics and consideration of Type IV hypersensitivity. Sharing such cases contributes to increased clinical awareness.

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### Introduction

Classified by Gell and Coombs into Types I-IV, hypersensitivity reactions are exaggerated immune responses to antigens. Type IV hypersensitivity is known as delayed-type hypersensitivity, characterized by cell-mediated immune responses. These reactions appear hours or days after contact with the antigen and typically involve an inflammatory process driven by T-lymphocytes.

Local anesthetics are widely used, especially in dental and minor surgical procedures and categorized into two main groups: esters and amides. Prilocaine is an amide-type local anesthetic and generally demonstrates a safe profile, although it may sometimes cause allergic reactions. While most allergic reactions are seen as Type I hypersensitivity, Type IV reactions can also occur.

This case report presents a rare prilocaine allergy manifesting as a Type IV hypersensitivity reaction and discusses

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the diagnostic and management process. Sharing such cases is highly important for increasing clinical awareness, avoiding misdiagnosis, and evaluating alternative treatment options.

### Case presentation

A 30-year-old male patient who had undergone repeated surgeries for lipoma on both forearms presented with skin lesions that appeared postoperatively, characterized by redness, itching, burning, and bruising, persisting for approximately three weeks (Figure 1). It was initially unclear whether these lesions were allergic in nature or due to the surgical procedure itself. In addition to local anesthetics, the patient had also received drugs such as midazolam and paracetamol during some of the operations.

Electrocautery pads and poliglecaprone sutures were used during surgery, while skin antiseptics containing 10% povidone-iodine and polyiodine were applied during wound care.

At the time of presentation to our reference center, there were no active skin lesions on the forearm; 4 months had passed since the most recent reaction. Laboratory evaluations prior to testing showed normal liver and kidney function tests. Creatine kinase was elevated at 381 U/L (reference: 0-171), tryptase at 4.85 µg/L, eosinophils at 70/mm<sup>3</sup>, and total immunoglobulin E (IgE) at 40 IU/mL. The patient had a known history of allergic asthma but none of chronic spontaneous urticaria, angioedema, or eczema.

Skin prick, intradermal, and delayed readings were performed for general anesthetic agents. Skin prick tests (SPTs) were done with atropine sulfate (0.25 mg/mL), pethidine hydrochloride (50 mg/mL), thiopental sodium (25 mg/mL), tramadol hydrochloride (50 mg/mL), midazolam (5 mg/mL), fentanyl (0.05 mg/mL), neostigmine methyl sulfate (0.5 mg/mL),

rocuronium bromide (10 mg/mL), propofol (10 mg/mL), povidone 10% (nondiluted form), and latex. The tests were positive for pethidine hydrochloride and atropine and negative for others. Intradermal tests showed positivity for tramadol hydrochloride and rocuronium bromide, and all agents showed negative delayed readings.

Skin testing for local anesthetics started with prick tests for lidocaine, prilocaine, and mepivacaine. SPT was performed in nondiluted form with a positive histamine control (10 mg/mL) and a negative saline control (0.9%). Positive SPT was defined as a wheal diameter at least 3 mm greater than the negative control after 20 minutes. If the SPT was negative, an intradermal test (IDT) was performed on the volar forearm at a 1:10 dilution, but as these tests were negative, they were conducted with a 1/10 dilution. Early readings were negative; however, at the 48th hour, hyperemia developed at the prilocaine injection site. At 120 hours, a slightly raised, erythematous lesion approximately 5-6 mm in diameter with mild surrounding redness and central edema was observed. On day 7, the lesion had evolved into a 1 cm diameter—a well-demarcated papulopustular erythematous area (Figure 2). Patch tests with lidocaine, prilocaine, and mepivacaine were applied to the patient's back at 10% concentrations. Erythema, edema, and a papular reaction were observed in the prilocaine test area at the 48-hour reading when the prilocaine allergy was confirmed (Figures 3 and 4). No reaction was observed in subcutaneous placebo and 0.1 cc and 1 cc provocation tests with mepivacaine. It is of importance as this patient is the first evaluated in literature due to allergic reaction to local anesthesia with very clear images.

### Discussion

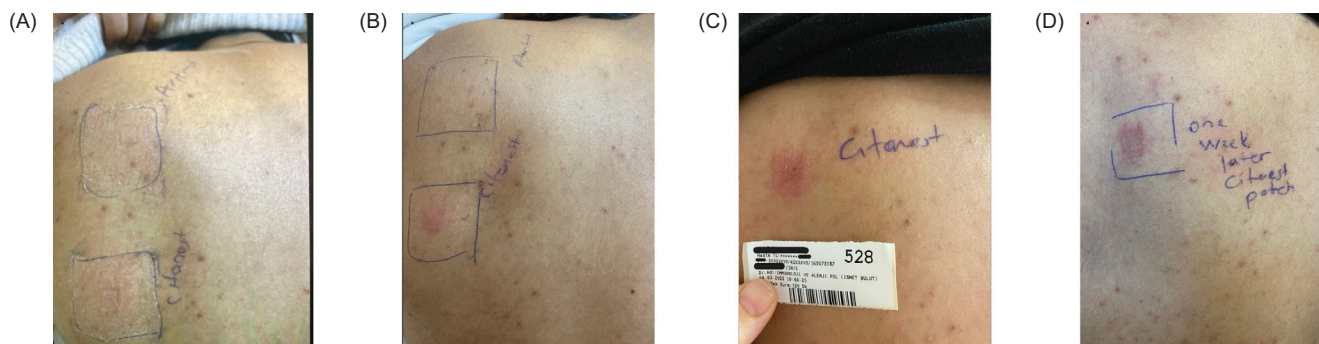
Allergic reactions to local anesthetics are quite rare, most commonly seen as Type I hypersensitivity. However, this case is notable in that it demonstrates a Type IV (delayed-type) hypersensitivity reaction to prilocaine, offering valuable insights into clinical practice.



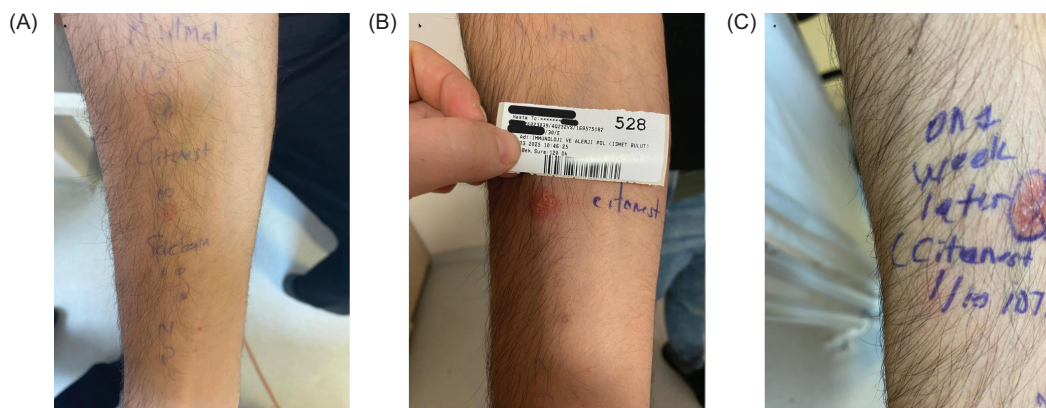
**Figure 1** Delayed-type skin reaction following surgical procedure. Inflammatory skin lesions with erythematous and edematous plaques developed on the forearm postoperatively.



**Figure 2** Delayed-type reaction findings to prilocaine. (A) Erythematous and edematous plaques on forearm on day 7 after intradermal prilocaine test. (B) Papulopustular lesion on day 7 at the prilocaine patch test site.



**Figure 3** Time-dependent progression of reaction at the patch test site. (A) No obvious reaction at the 24th hour. (B) Mild erythema at the prilocaine site at the 48th hour. (C) Persistent erythematous lesion at the 120th hour. (D) Distinct papulopustular lesion on day 7.



**Figure 4** Time-dependent progression of reaction at the intradermal test site. (A) Mild erythema at the 48th hour at the prilocaine site. (B) Increased erythema and edema at the 120th hour. (C) Prominent delayed-type inflammatory response on day 7.

Amide-type local anesthetics generally have a lower allergic potential compared to ester-type agents. This is primarily due to ester anesthetics being metabolized into para-aminobenzoic acid (PABA) derivatives, which are more allergenic.<sup>1</sup> Although prilocaine is an amide, allergic reactions have rarely been reported.<sup>2</sup>

Type IV hypersensitivity reactions are delayed inflammatory responses typically mediated by T-lymphocytes and clinically represented by conditions such as contact dermatitis or drug eruptions.<sup>3</sup> In our patient, the lack of immediate reaction and the appearance of erythematous and papulopustular lesions at 48 and 120 hours following intradermal testing with prilocaine are consistent with a classical Type IV pattern.

Patch testing and delayed intradermal readings are essential for diagnosing such reactions.<sup>4</sup> In our case, both tests confirmed the presence of a delayed hypersensitivity reaction to prilocaine.

There are very few cases in literature accounting for Type IV reactions to prilocaine. Some reports exist of contact dermatitis following topical application of prilocaine-lidocaine creams<sup>5,6</sup>; however, delayed reactions due to injected prilocaine are even rarer.<sup>7</sup>

Another noteworthy finding in our case was the continued progression of the skin reaction even at 120 hours and on the 7th day, with the lesion becoming centrally edematous and papulopustular, highlighting the persistent and evolving nature of delayed-type reactions.<sup>8</sup>

Recognizing these reactions is necessary for the prevention of readministration of the same agent in patients wrongly diagnosed as “nonallergic.”<sup>9</sup> Safe provocation testing with alternative local anesthetics (in this case, mepivacaine) plays a key role in treatment planning.<sup>10</sup>

## Conclusion

This case highlights the importance of recognizing Type IV hypersensitivity reactions to local anesthetics, particularly in patients with difficult-to-diagnose dermatological conditions. Rare allergic responses to commonly used agents like prilocaine should be clarified through comprehensive testing and safe alternatives should be identified. Awareness of such cases in clinical practice helps avoid unnecessary medications and ensures patient safety.

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## Authors' Consent for Publication

All authors have approved for this manuscript to be submitted for publication.

## Availability of Data and Materials

The data that support the findings of this study are not publicly available due to the information that could compromise the privacy of research participants, but are available from ÖA, MAT,YB, NY, ZYK, IB.

## Ethics Approval and Consent to Participate

This is a retrospective study with no ethics approval.

## Author Contributions

All authors had a part in the conceptualization; data curation; formal analysis; investigation; methodology; validation; visualization; and the writing of original draft.

## Conflicts of Interest

The authors have no conflicts of interest.

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