

Chlorhexidine Hypersensitivity: A Case Report of Delayed Reactions Associated with Epidermal Preparations

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Summary: Chlorhexidine is a topical antiseptic that is generally well tolerated in patients, making it a common preparatory substance in various surgical settings. Sparse case reports have identified immediate hypersensitivity reactions after exposure to this substance, especially in patients with a history of atopy. The purpose of this case report is to describe 3 unique presentations of delayed hypersensitivity to epidermal chlorhexidine preparation. Patients undergoing breast surgery by a single surgeon between December 2018 and January 2019 were retrospectively reviewed for incidence of dermatologic complications. Medical and surgical history of patients as well as dermatologic hypersensitivity course were collected. Three patients presented with a delayed hypersensitivity to the epidermal chlorhexidine surgical preparation, ChloraPrep. Each patient developed an erythematous, pruritic maculopapular rash in the distribution of the chlorhexidine application. This occurred beyond the immediate postoperative period—ranging from postoperative days 5 to 35. Initial treatment included the use of 1% hydrocortisone along with a systemic antihistamine. If there was no improvement in symptoms after 3 days, we transitioned patients to 0.5% triamcinolone ointment. If there was no improvement after 5 days on triamcinolone, the patient was reexamined and systemic steroids were prescribed. In each of our cases, all skin changes had resolved within 7–10 days of initial symptoms. Our findings highlight a series of delayed adverse reactions to epidermal chlorhexidine occurring beyond the intraoperative and immediate postoperative period. This case report serves to recognize a unique presentation pattern to ensure that all patients are accurately diagnosed and promptly treated via a systematic treatment algorithm. (*Plast Reconstr Surg Glob Open* 2020;8:e2945; doi: [10.1097/GOX.0000000000002945](https://doi.org/10.1097/GOX.0000000000002945); Published online 14 August 2020.)

Chlorhexidine is an antiseptic commonly used to prepare skin and mucous membranes for surgical procedures. As its use increases secondary to a generally favorable toxicity profile, reports of adverse reactions are increasing.¹ Epidermal chlorhexidine preparations have produced a gradient of adverse reactions ranging from mild hypersensitivity to severe anaphylaxis.^{2,3} The cases

presented in this report add to the limited body of knowledge about delayed hypersensitivity to preoperative application of epidermal chlorhexidine.

CASES

Case 1

A 19-year-old woman underwent bilateral reduction mammoplasty in January 2019. The chest, upper abdomen, and neck were prepared with ChloraPrep following manufacturer's instructions. The patient's medical history included Hashimoto's thyroiditis. She had no allergies and did not take medications.

On postoperative day 10, the patient returned to clinic with a 2-day history of maculopapular rash over bilateral breasts, neck, and trunk. The pruritic rash extended to the upper abdomen and the lower neck in the distribution

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of chlorhexidine application. The patient used a topical steroid cream with some relief. She was prescribed oral corticosteroids and was continued on topical steroids for 3 days, followed by Aquaphor. The patient returned to clinic on postoperative day 18 with complete resolution of the rash.

Case 2

A 40-year-old woman underwent a partial mastectomy with oncoplasty and contralateral breast reduction in the setting of ductal carcinoma in situ in January 2019. The chest was prepared with ChloraPrep following manufacturer's instructions. The patient's medical history included hypothyroidism. Her past surgeries were without complications. She reported hives with penicillin, contact dermatitis secondary to adhesives, and an unspecified allergy to naprosyn. Of note, no adhesives were used on the breast.

On postoperative day 5, the patient noted an erythematous rash on bilateral breasts. The patient was prescribed triamcinolone topical steroid cream and a course of oral steroids. The rash progressively resolved, and physical examination on postoperative day 17 was normal (Fig. 1).

Case 3

A 54-year-old woman with invasive ductal carcinoma of the left breast underwent a modified radical mastectomy with immediate tissue expander placement in December 2018. Similarly, the chest was prepared with ChloraPrep following manufacturer's instructions. Her surgical history included a lumpectomy done 2 decades before without complications. The patient reported unspecified allergies to sulfonamide-containing medications.

On postoperative day 35, the patient reported a pruritic and erythematous maculopapular rash on the central aspect of her chest. The rash extended from the lateral, superior, and inferior left breast to the upper abdomen, again in the distribution of chlorhexidine skin preparation application. The patient's primary care physician prescribed mometasone furoate topical corticosteroids. The patient reported improvement with persistent pruritus for several days before complete resolution. She was not seen in clinic for follow-up due to self-reported clearance of symptoms (Fig. 2).

DISCUSSION

Chlorhexidine in its various preparations has become a commonplace antiseptic. Despite its generally well-tolerated toxicity profile, there are case reports of adverse reactions to this substance. This case report adds to the knowledge of delayed hypersensitivity reactions to topical chlorhexidine, raises awareness of its clinical presentation, and provides a novel algorithm for treatment.

Previous case reports concerning delayed hypersensitivity to topical chlorhexidine describe symptoms in the near postoperative period.^{4,5} These reactions were characterized by the development of an intense, erythematous rash within 48 hours of operation and were successfully treated with topical or oral steroids.^{4,5} The cases described above broaden this presentation. Our patients developed



Fig. 1. Image of delayed hypersensitivity to epidermal chlorhexidine preparation in case 2. This erythematous rash developed on bilateral breasts on postoperative day 5 and cleared with a topical steroid application. Of note, no adhesives were used on this patient and no signs of infection were present.



Fig. 2. Image of delayed hypersensitivity to epidermal chlorhexidine preparation in case 3. The patient noted a pruritic, erythematous maculopapular rash >1 month from her operative date. Symptoms cleared with application of topical steroids. Once again, no adhesives were used on this patient and no signs of infection were present.

rashes between postoperative days 5 and 35. In each case, the distribution of the dermatitis paralleled the application of ChloraPrep.

Although the underlying mechanism of these reactions is not fully understood, Dick et al⁵ have proposed a mechanism of sensitization. The authors noted that prolonged exposure to ChloraPrep due to inadequate postoperative cleansing of the region may have sensitized their patient. Two of our patients had previous surgeries;

thus, possible sensitization may have contributed to their delayed hypersensitivity reaction. Our third patient may have been sensitized via an alternate route, due to the widespread inclusion of chlorhexidine in nonsurgical products. Exposure to chlorhexidine via surgical or nonsurgical chlorhexidine-containing products may contribute to delayed hypersensitivity reactions, even 1 month postoperatively.

The true incidence of allergy to chlorhexidine remains unknown and may be underreported.³ Patch testing has demonstrated a positive reaction in 0.24%–2% of individuals,^{6,7} with an even higher incidence in patients with a history of atopic dermatitis, leg ulcers, and leg eczema.^{7–9} These individuals, in addition to those previously sensitized to chlorhexidine, are particularly susceptible to developing an adverse reaction to chlorhexidine later in life.⁴ It is important to be aware of the potential reaction to chlorhexidine preparations secondary to its widespread inclusion in products and increasing likelihood of previous sensitization.

In our practice, we routinely use chlorhexidine preparation in surgical patients who have no open wounds or contraindications. We follow the manufacturer's application recommendations, and the region is cleaned postoperatively with saline before dressing. We routinely see patients within 1 week of operation. If a rash is noted or reported, the patient is examined. A topical steroid, hydrocortisone 1%, and a systemic antihistamine are recommended. If there is no improvement within 3 days, we transition to triamcinolone 0.5% ointment. If symptoms do not improve after 5 days on triamcinolone, the patient is examined and systemic steroids are prescribed. In our practice, skin changes have all resolved within 7–10 days of initial symptoms, with no evidence of prolonged skin changes or ulceration.

One limitation of our study is the absence of postoperative intradermal allergy testing. Such a test could confirm the described association while ruling out other possible etiologies. We believe future studies and treatment

protocols could incorporate formal patch sensitivity testing or referral to a dermatologist for patients with suspected allergy to chlorhexidine.

SUMMARY

These findings highlight the possibility of an adverse reaction developing beyond the immediate postoperative period. This underscores the importance of counseling patients on all possible adverse reactions following surgery and demonstrates the necessity of close postoperative follow-up for surgical patients.

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