Life after patch testing: Allergic contact dermatitis caused by propylene glycol in Vivelle transdermal estradiol patch

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INTRODUCTION

Vivelle is a transdermal estradiol patch with applications in both the treatment of menopause and maintenance of pregnancy in patients undergoing in vitro fertilization (IVF). Transdermal patches commonly provoke irritant contact dermatitis or, rarely, allergic contact dermatitis (ACD) caused by the patch components. Herein, we report a novel case of ACD caused by the excipient propylene glycol of the Vivelle estradiol patch in a patient undergoing assisted reproductive therapy.

Abbreviations used:

ACD: allergic contact dermatitis
IVF: in vitro fertilization

CASE REPORT

A 39-year-old woman with a medical history of anovulatory infertility secondary to functional hypothalamic amenorrhea was started on Lupron and progesterone injections, Vivelle transdermal estradiol patch, and Medrol pill as part of an IVF treatment cycle. Within 2 months, she developed a papulovesicular eruption within the patch application sites, as well as a more generalized truncal eruption, including at sites of intramuscular progesterone injection. Her symptoms continued to worsen despite switching to vaginal progesterone gel. After suffering a miscarriage, the patient was referred for patch testing prior to initiating another round of IVF.

Patch testing was performed with the North American Contact Dermatitis Group Standard Allergens, an acrylate series, the patient's personal products, as well as the progesterone solution, individual excipients, and the Vivelle transdermal patch itself. The Vivelle transdermal estradiol patch is a three-layer transdermal system, composed of a backing, an adhesive impregnated with estradiol, and protective liner. The backing is a translucent and flexible film comprised of ethylene vinyl alcohol copolymer film, polyurethane film, urethane polymer, and an epoxy resin. The middle adhesive layer contains estradiol, acrylic adhesive, polyisobutylene, ethylene vinyl acetate copolymer, 1,3-butylene glycol, styrene-butadiene rubber, oleic acid, lecithin, propylene glycol, bentonite, mineral oil, and dipropylene glycol. Finally, the protective liner is a polyester release liner removed before the system is applied to the skin.

At 120 hours, the patient was noted to have a 2+ reaction to propylene glycol (30.0% aqueous) as well as a 3+ reaction to the Vivelle estradiol patch itself. Notably, she did not react to injectable progesterone, intravaginal progesterone gel, or other drug excipients such as benzyl alcohol, bisphenol, an epoxy resin, or any acrylates. Furthermore, subsequent intradermal tests for progesterone itself was negative. She exhibited several other reactions, none of which were felt to be clinically relevant to this episode of dermatitis.

Based on these results and a review of all personal products and medication exposures, the patient was diagnosed with ACD caused by propylene glycol in the transdermal patch. She was subsequently able to tolerate intramuscular injections of estradiol valerate and progesterone without recrudescence of her rash and ultimately delivered a full-term pregnancy after a successful round of IVF.

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DISCUSSION

Transdermal patches offer several advantages over conventional routes of drug delivery, including non-invasive administration, more stable drug levels, and improved compliance, tolerability, and bioavailability.[1] There have been a few reports of ACD caused by estradiol itself,[2-5] as well as by excipients such as ethanol and hydroxypropyl cellulose within these patches.[6] To our knowledge, this is the first report of a case of ACD due to the excipient propylene glycol in a transdermal estradiol patch. Propylene glycol is a widely used emollient and emulsifier with well-established irritant and allergic potential.

Current strategies for managing irritant contact dermatitis due to transdermal patches include patch application site rotation, shorter application intervals, and pre-application of clobetasol. For ACD, patients can take antihistamines, use alternative formulations, or switch from transdermal administration to oral ingestion or intramuscular injections of the same drug if the excipient and not the drug itself is the true etiology of the ACD.

This case highlights the life-altering, potentially life-giving, role of patch testing in the diagnostic evaluation of ACD. Patients using transdermal hormone patches who present with eczematous eruptions should be referred for patch testing, which in some cases may allow reformulation of their assisted reproductive therapy regimens to enable successful conception.

Conflicts of interest

None disclosed.

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