Allergic contact dermatitis of adjacent normal skin from 5-fluorouracil for the treatment of flat facial warts

Usman Asad, BS^a , Jeannie Nguyen, MD^b , and Ashley Sturgeon, MD^b

^aSchool of Medicine, Texas Tech University Health Sciences Center, Lubbock, Texas; ^bDepartment of Dermatology, Texas Tech University Health Sciences Center, Lubbock, Texas

ABSTRACT

Topical 5-fluorouracil has proven to be an effective treatment for flat warts. Although cases of local irritation at the site of application have been reported, allergic contact dermatitis on the adjacent normal skin is generally uncommon. Reactions to propylene glycol and stearyl alcohol, two vehicle components of 5-fluorouracil, have also been described. In this report, we present a 21-year-old woman who developed allergic contact dermatitis of the adjacent normal skin after topical application of 5-fluorouracil to the face for the treatment of flat warts.

KEYWORDS Allergic contact dermatitis; 5-fluorouracil; rash; warts

Flat warts (*Verruca plana*) are reddish-brown or flesh-colored well-demarcated, hyperkeratotic, flat-topped papules characterized by minimal scaling and mild elevation.¹ 5-Fluorouracil (5-FU) treats flat warts by acting as an irritant eliciting an immune response. Allergic contact dermatitis of the adjacent normal skin, defined as skin that has not been treated with 5-FU but is adjacent to skin that has been treated, is caused by a hypersensitivity reaction involving T lymphocytes and cytokines. Common manifestations include local pain, pruritus, blister and vesicle formation, eczematous eruptions, and extensive ulcerations.² In this report, we describe a woman who developed allergic contact dermatitis of the adjacent normal skin after topical application of 5-FU to treat flat facial warts.

CASE DESCRIPTION

A 21-year-old white woman presented with an 18-month history of flat facial warts. Imiquimod and cryotherapy had failed to alleviate her symptoms. Her medical history was otherwise significant for acne vulgaris and hypothyroidism. Her daily medications included tretinoin cream, levothyroxine, oral contraceptive pills, and spironolactone. On examination, she had 15 flesh-colored papules measuring 3 to 6 mm on her forehead, chin, and jawline. At that visit, she was treated with intralesional Candin injection and was

prescribed 5% 5-FU (Efudex) cream. After one application of the cream, she reported severe erythema, irritation, and ulceration to the adjacent normal skin and discontinued the 5-FU (*Figure 1*). At her 4-week clinic follow-up appointment, irregular erythematous patches and plaques on her forehead and cheeks with erosions were noted. A diagnosis of allergic contact dermatitis of the normal adjacent skin due to 5-FU was made; she was prescribed oral doxycycline, hydrocortisone 2.5% cream, and topical mupirocin. She showed improvement on subsequent follow-up and was advised to treat her facial warts with tretinoin cream and cryotherapy.

DISCUSSION

5-FU has proven to be a safe and effective treatment for flat warts, both as monotherapy and combination therapy.^{3–5} Cases of irritant contact dermatitis localized to the site of 5-FU application have been reported; adverse effects have included hyperpigmentation, dryness, and erythema.⁶ However, allergic contact dermatitis on the adjacent normal skin from 5-FU is generally uncommon. In the few reported cases of allergic contact dermatitis, symptoms have included erythema, ulcerations, severe pruritus, and eczematous eruptions. We favored the diagnosis of allergic contact dermatitis over irritant contact dermatitis because our patient's rash was widespread and present beyond the

Corresponding author: Jeannie Nguyen, MD, Department of Dermatology, Texas Tech University Health Sciences Center, 3601 4th Street, Lubbock, TX 79430 (e-mail: Jeannie.Nguyen@ttuhsc.edu)

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Figure 1. (a) A 21-year-old woman with multiple irregular erythematous patches and plaques with erosions distributed bilaterally on her forehead and cheeks after one application of 5-fluorouracil 5% cream. (b) Multiple 2–15 mm erythematous macules, patches, papules, and plaques on the face at 6-week follow-up.

sites of 5-FU application. In addition, her rash was more severe and extensive than the irritant reaction seen from 5-FU, which generally does not consist of severe erythema, ulcerations, or erosions.

Reactions to propylene glycol and stearyl alcohol, two vehicle components of Efudex, have also been described.^{7,8} Sensitization to 5-FU has been seen after reinitiating previous treatment, with long-term therapy, or with occlusive treatments.^{9,10} However, none of these situations applied to our patient, as this was her first use of 5-FU. Patch testing can confirm the diagnosis but has the possibility of being falsely negative; one-fourth of patients may escape detection, requiring intradermal testing.¹¹ 5-FU is considered a weak sensitizer; the therapeutic inflammation produced by 5-FU may enhance penetration through the skin, thereby increasing the atopic potential of allergens.¹²

In conclusion, allergic contact dermatitis of the normal adjacent skin should be considered in the presence of severe pruritus, eczematous or erythematous eruptions, or ulcerations to the adjacent normal skin after application of topical 5-FU. Our patient experienced severe distress from the reaction. Her condition negatively affected her self-esteem, confidence, and quality of life. A careful history of previous allergic reactions, as well as prompt treatment upon evidence of a reaction, is highly recommended to reduce the risk of scarring and maximize the individual's medical and psychological well-being.

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ORCID

Usman Asad <http://orcid.org/0000-0002-0996-2834>

Jeannie Nguyen <http://orcid.org/0000-0001-5965-3098>

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