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Case Report

Allergic Contact Dermatitis to Efudex™ Cream Diagnosed by ROAT

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Abstract

Efudex cream (5-fluorouracil, 5-FU) is a topical antimitotic chemotherapy indicated for the treatment of actinic keratoses and superficial basal cell carcinomas, but has also been used to treat other malignant and non-malignant skin lesions. Although Efudex commonly induces an irritant contact dermatitis in lesional skin at the site of application, allergic contact dermatitis (ACD) is not frequently reported. ACD is diagnosed via epicutaneous patch testing, in which standardized chemicals are applied to the skin and evaluated by a standard protocol. There are commercially available patch test kits, but these may not contain the specific components in a topical preparation in question and more comprehensive. Furthermore, more specialized patch testing my not be readily available or economically prudent. In this report, the authors present a case of ACD to Efudex cream diagnosed by repeated open application test (R.O.A.T.) and supported by limited patch testing.

Keywords: Contact dermatitis; R.O.A.T; Efudexl; Actinic Keratosis

Case Report

A 62-year-old Caucasian male with no prior history of skin cancer or other skin disease presented with extensive actinic keratoses on his forearms with predominance on the left side. He had previously used 5-fluorouracil (Efudex™, Valeant Pharmaceuticals, and Montreal, Canada) the year before and reported that he had had a painful and brisk response. Because of his history, he was prescribed a course of topical 5% 5-fluorouracil (Efudex) cream twice a day for two weeks, to be applied solely to the left forearm. On day 7, the patient presented to clinic, he had developed a painful, eczematous dermatitis with microvesiculation, at the site of application. An ACD to Efudex cream was suspected. The Efudex was discontinued and the patient started on triamcinolone 0.1% ointment. At follow-up six weeks later, a repeat open application test (R.O.A.T.) with Efudex was done near the sun-protected medial aspect of the antecubital fossa of the right arm, which was specifically devoid of actinic keratoses. The patient was instructed to apply Efudex cream to a marked 3 x 3 cm patch, twice a day for 7 days. The patient then returned to clinic on final day of R.O.A.T. testing and was found to have developed with a highly pruritic, eczematous dermatitis at the site of application on his right antecubital fossa, which correlated with a rebound flare of the dermatitis on his left forearm, where he had applied Efudex six weeks earlier. Several of the excipients in Efudex cream (standardized allergens we have available for testing) were subsequently patch tested, including stearyl alcohol 30% petrolatum, propylene glycol 30% aqueous (in duplicate), polysorbate 60 petrolatum and parabens 12% petrolatum. All excipient patches were observed to be negative at 48, 72 and 120 hours, further suggesting the role of the active ingredient 5-FU in the observed ACD.

Discussion

Efudex cream, a topical antimitotic chemotherapy used for the treatment of actinic keratoses and superficial basal cell carcinomas [1] is an uncommon sensitizer, but nevertheless, ACD has been described in the literature.

Sensitization can occur to the active ingredient, 5-FU [2,3], or to one of the cream's vehicle components, including stearyl alcohol [4,5] and propylene glycol [6]. That said, there is some thought that the incidence of 5-FU ACD is actually quite high, and Goette et al. proposed that hypersensitivity may contribute to the mechanism of action in the destruction of abnormal cells [7]. With topical treatments that are designed to cause a visible skin reaction, it is important to differentiate between a very brisk therapeutic response and a true contact allergy to a substance. The development of a

Figure 1: Positive repeated open application test with 5% Efudex cream on volar forearm. Note the reaction distal to the application site due to transfer of Efudex from bending of the arm.

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severely pruritic, eczematous dermatitis at the site of application 48 to 120h after application of a substance, or the development of a pruritic dermatitis at a distant site (as was seen in our patient), suggests an allergic reaction rather than local irritation [2].

R.O.A.T is a variation of a use test, which aims to replicate the mode and frequency of commonly prescribed application [8]. This case illustrates that R.O.A.T. can be a valuable tool in the diagnosis of contact allergy for physicians who do not have the resources to perform the extended patch tests or when a patch test yields negative results. Unfortunately, patients who have had severe adverse reactions to a topical medication would oftentimes prefer to avoid future contact with the medication altogether, thus it is not always feasible to test to differentiate between a true allergy and a vigorous reaction. In this case, the patient was instructed to perform R.O.A.T. to his antecubital fossa, however in hindsight we recommend that irritating substances such as 5-FU be applied to regions of skin other than flexural areas, thus avoiding increased absorption where skin to skin contact results in occlusion.

Conflicts of Interest

The authors have no financial disclosures or other conflicts of interest to report relating to the content of this article.

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