

# Fluorouracil cream induced scarring alopecia after topical treatment of squamous cell carcinoma in situ



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**Key words:** 5-fluorouracil; adverse effects; alopecia; chemotherapy-induced alopecia; cicatricial alopecia; drug-induced; Efudex; fluorouracil; hair loss; permanent chemotherapy-induced alopecia; scarring alopecia.

## INTRODUCTION

Actinic keratoses (AKs) and squamous cell carcinomas arise on sun-exposed skin and are treated with different modalities that include light-based, topical, destructive, and surgical modalities.<sup>1</sup> One commonly used topical therapy is 5% 5-fluorouracil (5-FU) cream that frequently causes brisk dermatitis. This report discusses a case of a man in whom scarring alopecia developed after treatment with topical 5-FU.

## CASE REPORT

An 85-year-old man with a long history of non-melanoma skin cancers presented for Mohs consultation. He had squamous cell carcinoma in situ (SCCIS) of the lateral aspect of the left eyebrow diagnosed through biopsy by an outside dermatologist (Fig 1). Physical examination showed diffuse actinic damage of the lateral aspect of the left eyebrow; however, the carcinoma was not easily identified. A joint decision was made to treat the left eyebrow with 5-FU cream twice daily for 2 weeks to treat the overlying AKs and reevaluate the area for surgical planning.

The patient returned for reevaluation after 2 weeks of treatment. Treatment with 5-FU significantly improved the actinic damage; however, the SCCIS site was again not easily identifiable. The plan was then to treat the underlying SCCIS with 5-FU twice daily for an additional 10 weeks, with a total goal of 12 weeks. After 12 weeks of 5-FU treatment, there was minimal erythema of the treated area, with clinical clearance of the previously biopsied SCCIS

### Abbreviations used:

5-FU:	5-fluorouracil
AK:	actinic keratosis
PCIA:	permanent chemotherapy-induced alopecia
SCCIS:	squamous cell carcinoma in situ



**Fig 1.** Diffuse actinic damage of the lateral aspect of the left eyebrow with blue outlined biopsy site (picture from an outside provider).

and AKs (Fig 2, A). On examination, hair loss on the lateral aspect of the left eyebrow with minimal terminal hairs medially was also noted. The patient then returned for the 6-month follow-up with no hair regrowth (Fig 2, B).

On examination, there was a loss of follicular ostia on trichoscopy (Fig 3). A 3-mm punch biopsy confirmed the loss of follicular units and fibrosis consistent with scarring alopecia (Fig 4).

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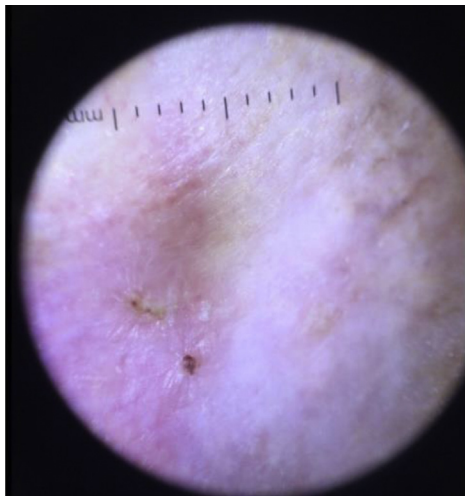
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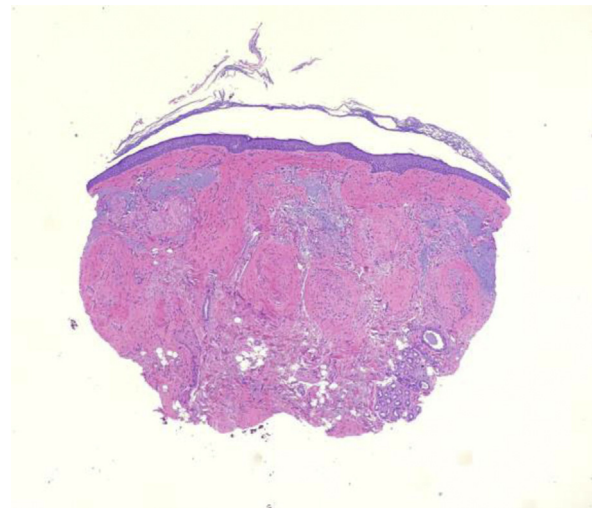
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**Fig 2.** **A**, At 12 weeks after 5-FU treatment, localized alopecia of the lateral aspect of the left eyebrow with erythema and minimal terminal hairs medially was observed. **B**, At 6 months after 5-FU treatment, localized alopecia of the lateral aspect of the left eyebrow with minimal terminal hairs medially was observed.



**Fig 3.** Trichoscopy of the lateral aspect of the left eyebrow with loss of follicular ostia.



**Fig 4.** Pathology showing no viable follicles or sebaceous glands with fibrous tracts within the dermis.

## DISCUSSION

AKs are epidermal neoplasms that have the potential to progress into SCCIS, which may be a precursor to invasive squamous cell carcinoma.<sup>1,2</sup> Because of this malignant transformation potential, early intervention is indicated. AKs and squamous cell carcinomas typically occur on sun-exposed skin such as the face, scalp, forearms, and hands.<sup>1</sup> Topical agents such as 5-FU have been approved for the treatment of both AKs and SCCIS.<sup>2</sup>

5-FU, a fluoropyrimidine antineoplastic drug, is an effective topical treatment used for various dermatologic and neoplastic disorders. When entering the cell, 5-FU inhibits thymidylate synthase, thereby blocking DNA synthesis.<sup>1,3,4</sup> This disruption preferentially targets rapidly proliferating cells.<sup>3,4</sup> Patients typically report brisk dermatitis, which includes pain, pruritus, erythema, irritation, erosion, crusting, and eczematous reaction.<sup>5</sup> Rare side effects include temporary hair loss, allergic contact

dermatitis, wound infections, erysipelas, ulcers, neutropenia, and angioedema.<sup>4,5</sup> This case describes a potential side effect of scarring alopecia.

Hair grows in a cyclic fashion and includes 3 phases: anagen (growth), catagen (regressing), and telogen (resting). The anagen hair follicle bulbs have rapidly dividing matrix keratinocytes. This increased mitotic activity makes the anagen hair bulbs more susceptible to the effects of 5-FU.<sup>6</sup>

Many systemic chemotherapies have been reported to target the anagen hair cycle, frequently causing anagen effluvium, a nonscarring alopecia that is temporary and regrows. Permanent chemotherapy-induced alopecia (PCIA) has been increasingly reported and is commonly associated with systemic breast cancer therapies.<sup>7</sup> The mechanism of action of PCIA is not yet clear; however, it is thought to be caused by toxic damage to the hair follicle stem cells.<sup>7</sup> One study examined 10 histologic cases of scalp PCIA secondary to systemic chemotherapy and found that all specimens had a non-scarring pattern with a preserved number of follicular units and no fibrosis.<sup>8</sup> Thus, in this cohort, PCIA was not caused by scarring alopecia, which is characterized by the destruction of the hair follicle unit. Whereas in our patient, trichoscopy and dermatopathology confirmed a scarring process and, therefore, irreversible hair loss.

To our knowledge, this is the first report of scarring alopecia secondary to topical 5-FU described in the literature. The etiology of this alopecia is uncertain, as is how frequently it occurs. It is important for dermatologists to understand this

potential adverse reaction and counsel patients accordingly.

#### Conflicts of interest

None disclosed.

#### REFERENCES

1. Hashim PW, Chen T, Rigel D, Bhatia N, Kircik LH. Actinic keratosis: current therapies and insights into new treatments. *J Drugs Dermatol*. 2019;18(5):s161-s166.
2. Shimizu I, Cruz A, Chang KH, Dufresne RG. Treatment of squamous cell carcinoma in situ: a review. *Dermatol Surg*. 2011;37(10):1394-1411. <https://doi.org/10.1111/j.1524-4725.2011.02088.x>
3. Prince GT, Cameron MC, Fathi R, Alkousakis T. Topical 5-fluorouracil in dermatologic disease. *Int J Dermatol*. 2018; 57(10):1259-1264. <https://doi.org/10.1111/ijd.14106>
4. Cohen PR. Topical application of 5-fluorouracil 5 percent cream associated with severe neutropenia: discussion of a case and review of systemic reactions after topical treatment with 5-fluorouracil. *Dermatol Online J*. 2018;24(4):13030/qt974797j7.
5. Love WE, Bernhard JD, Bordeaux JS. Topical imiquimod or fluorouracil therapy for basal and squamous cell carcinoma: a systematic review. *Arch Dermatol*. 2009;145(12):1431-1438. <https://doi.org/10.1001/archdermatol.2009.291>
6. Rorex JN, Johnson-Jahangir H, Ferguson N. Transient chemotherapy-induced alopecia after intralesional 5-fluorouracil treatment of keloids. *JAAD Case Rep*. 2019;5(9):787-788. <https://doi.org/10.1016/j.jdc.2019.06.033>
7. Kang D, Kim IR, Choi EK, et al. Permanent chemotherapy-induced alopecia in patients with breast cancer: a 3-year prospective cohort study. *Oncologist*. 2019;24(3):414-420. <https://doi.org/10.1634/theoncologist.2018-0184>
8. Miteva M, Misciali C, Fanti PA, Vincenzi C, Romanelli P, Tosti A. Permanent alopecia after systemic chemotherapy: a clinico-pathological study of 10 cases. *Am J Dermatopathol*. 2011;33(4): 345-350. <https://doi.org/10.1097/DAD.0b013e3181f9c25>