

Transient chemotherapy-induced alopecia after intralesional 5-fluorouracil treatment of keloids



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INTRODUCTION

Keloids represent an abnormal response to wound healing that results in excess collagen formation.¹ Keloids occur more frequently in individuals with higher Fitzpatrick skin types after a traumatic event incites inflammatory reaction in the skin; although, keloids have been reported to arise spontaneously.¹ The elusive pathogenesis of keloids has allowed the use of multiple modalities in treatment. Currently, the use of intralesional 5-fluorouracil is efficacious in reducing the size and recurrence of keloids.² The antimetabolite blocks the synthesis of thymidine thereby inducing cell death. Reported side effects of intralesional 5-fluorouracil include temporary pain at the injection site, ulceration, and hyperpigmentation, all of which usually resolve. As a systemic antineoplastic treatment, fluorouracil has occasionally been associated with alopecia. We present a case of transient chemotherapy-induced alopecia occurring after intralesional 5-fluorouracil used to treat keloids on the right cheek of a bearded male. To our knowledge, this is the first report of alopecia occurring after localized intralesional chemotherapy treatment of keloids.

CASE REPORT

A 58-year-old man presented for evaluation of multiple keloid scars. He reported keloid development at a young age after having chicken pox. He continues to get new keloids with procedures but notes that they also develop spontaneously. The keloids are significantly symptomatic with reported pruritus and pain. Previously, he received multiple

Abbreviations used:

IL: interleukin
TGF: transforming growth factor

rounds of intralesional triamcinolone acetonide without benefit and excision of keloids, with recurrence. The patient reported being hospitalized after triamcinolone acetonide injections because of markedly elevated blood sugars occurring after diabetes development and adamantly refused further intralesional steroid therapy. He also received intralesional bleomycin for some keloids without benefit. Additional medical history included folliculitis and acne keloidalis nuchae, which was treated with minocycline, 100 mg twice daily, benzoyl peroxide wash, clindamycin solution, and clobetasol ointment.

Physical examination found innumerable brown-to skin-colored keloidal papules and plaques on the cheek, jawline, neck, scalp, chest, back, extremities, and suprapubic groin. The patient had symptomatic keloids on the right cheek treated with a total of 1 mL of intralesional fluorouracil (50 mg/mL) (Fig 1). The patient noted some redness and inflammation over the treated areas the next day, which resolved. At 6-week follow-up, he noted improvement in keloids and underwent a second treatment to the affected areas on the right cheek and to a keloid on the right upper arm. During the next 4 weeks (10 weeks after initial treatment), he noted hair loss over the beard area on the right cheek surrounding the keloids previously treated with intralesional fluorouracil

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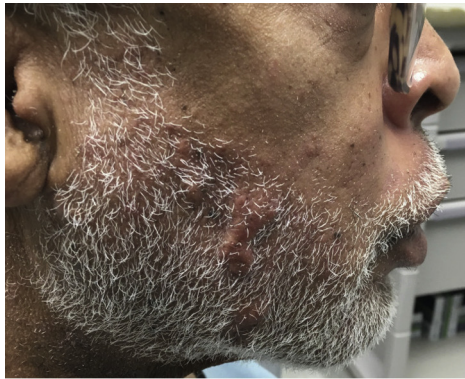


Fig 1. Brown keloidal plaques on the right cheek consistent with keloid scarring. Photograph represents keloids before treatment in this Fitzpatrick type V patient.

(Fig 2). Hair loss was noted to be temporary; hair regrew several weeks after completion of intralesional chemotherapy injections on the cheek.

DISCUSSION

The pathogenesis of keloids remains to be understood; however, it was proposed that keloids form secondarily to dysregulation of the inflammation phase of wound healing.³ Normal wounds heal through the predictable and overlapping phases of inflammation, proliferation, and maturation. It is proposed that excess proinflammatory cytokines interleukin (IL)-6 and IL-8, transforming growth factor (TGF)- β 1 and TGF- β 2, and perhaps a deficiency of the anti-inflammatory IL-10 and TGF- β 3, contribute to the aberrant scar formation.³ Particularly, fibroblast within keloids are more responsive to the growth factors resulting in increased collagen formation. The excessive activity of fibroblasts is thought to be suppressed by the antimetabolite 5-fluorouracil.⁴ The cytotoxicity of the nucleoside analogue stems from its inhibition of thymidylate synthase and the incorporation of its metabolites into DNA.⁵ These processes damage DNA leading to the eventual induction of apoptosis via p53 activation. Given the fact that fluorouracil affects rapidly proliferating cells, the rapidly dividing matrix keratinocytes in the bulb region of the anagen hair follicle are uniquely vulnerable.

The hair cycle involves 3 distinct phases: anagen (growth), catagen (regression), and telogen (resting). The anagen phase of the hair cycle lasts for years and is a time when the matrix keratinocytes have markedly increased mitotic activity.⁶ Catagen is a 2- to 3-week process in which the proximal portion of the follicle regresses, whereas telogen is a time of



Fig 2. Localized nonscarring alopecia noted several weeks after treatment with intralesional 5-fluorouracil. There is a noted reduction in the size of the keloids with overlying hyperpigmentation.

quiescence lasting months. It has been proposed that alopecia secondary to systemically administered chemotherapeutics targets the anagen phase, as keratinocytes are susceptible to damage during this time. The degree of damage to the hair follicle stem cells determines whether hair loss will be reversible or permanent.⁶ Fluorouracil, when given systemically, induces alopecia less frequently and with milder effects compared with other chemotherapeutic agents.⁶ The transient nature of hair loss noted in our patient suggests that the 5-fluorouracil did not permanently affect these stem cells. To our knowledge, transient localized alopecia secondary to intralesional fluorouracil during treatment of keloids has not been previously discussed. Dermatologists should be aware of this potential side effect and counsel patients accordingly.

REFERENCES

1. English RS, Shenefelt PD. Keloids and hypertrophic scars. *Dermatol Surg.* 1999;25(8):631-638.
2. Kontochristopoulos G, Stefanaki C, Panagiotopoulos A, et al. Intralesional 5-fluorouracil in the treatment of keloids: an open clinical and histopathologic study. *J Am Acad Dermatol.* 2005; 52:474-479.
3. Berman B, Maderal A, Raphael B. Keloids and hypertrophic scars: pathophysiology, classification, and treatment. *Dermatol Surg.* 2017;43.
4. Nanda S, Reddy BSN. Intralesional 5-fluorouracil as a treatment modality of keloids. *Dermatol Surg.* 2004;30(1):54-57.
5. Longley DB, Harkin DP, Johnston PG. 5-fluorouracil: mechanisms of action and clinical strategies. *Nat Rev Cancer.* 2003;3(5): 330-338.
6. Paus R, Haslam IS, Sharov AA, Botchkarev VA. Pathobiology of chemotherapy-induced hair loss. *Lancet Oncol.* 2013;14: e50-e59.