

Postinflammatory Hyperpigmentation Following Treatment of Hyperkeratosis Lenticularis Perstans With Tazarotene Cream 0.1%

Kristyna Gleghorn, MD; Tanya Riddle, MD; Adrian Subrt, MD; Erica Kelly, MD

PRACTICE POINTS

- Hyperkeratosis lenticularis perstans is a rare keratinization disorder that presents with asymptomatic red-brown papules with irregular horny scales on the lower extremities.
- Hyperkeratosis lenticularis perstans can be difficult to diagnose and treat. Hematoxylin and eosin staining generally will show hyperkeratosis and parakeratosis with basal layer degeneration and a perivascular lymphocytic infiltrate.
- Tazarotene cream 0.1% is a synthetic retinoid sometimes used for treatment of hyperpigmentation, but it also can cause postinflammatory hyperpigmentation.

To the Editor:

Hyperkeratosis lenticularis perstans (HLP), or Flegel disease, is a rare keratinization disorder characterized by asymptomatic, red-brown, 1- to 5-mm papules with irregular horny scales commonly seen on the dorsal feet and lower legs.¹ Hyperkeratosis lenticularis perstans is notorious for being difficult to treat. Various treatment options, including 5-fluorouracil, topical and oral retinoids, vitamin D₃ derivatives, psoralen plus UVA therapy, and dermabrasion, have been explored but none have proven to be consistently effective.

A woman in her 50s presented with an asymptomatic eruption on the legs and thighs that had been present for the last 20 years. She had been misdiagnosed by multiple outside providers with atopic dermatitis and was treated with topical steroids without considerable improvement.

Upon initial presentation to our clinic, physical examination revealed a woman with Fitzpatrick skin type II with multiple hyperpigmented, red-brown, 2- to 6-mm papules on the extensor surfaces of the lower legs and upper thighs (Figure, A). A 3-mm punch biopsy of a lesion on the right upper thigh revealed hyperkeratosis and parakeratosis with basal layer degeneration and a perivascular lymphocytic infiltrate. The clinical and histopathologic findings were consistent with HLP.

The patient was started on treatment with 5-fluorouracil cream on the right leg and tazarotene cream 0.1% on the left leg to determine which agent would work best. After 9 weeks of treatment, slight improvement was observed on both legs, but the lesions were still erythematous (Figure, B). Treatment was continued, and after 14 weeks complete resolution of the lesions was noted on both legs; however, postinflammatory hyperpigmentation (PIH) was observed on the left leg, which had been treated with tazarotene (Figure, C). The patient was lost to follow-up prior to treatment of the PIH.

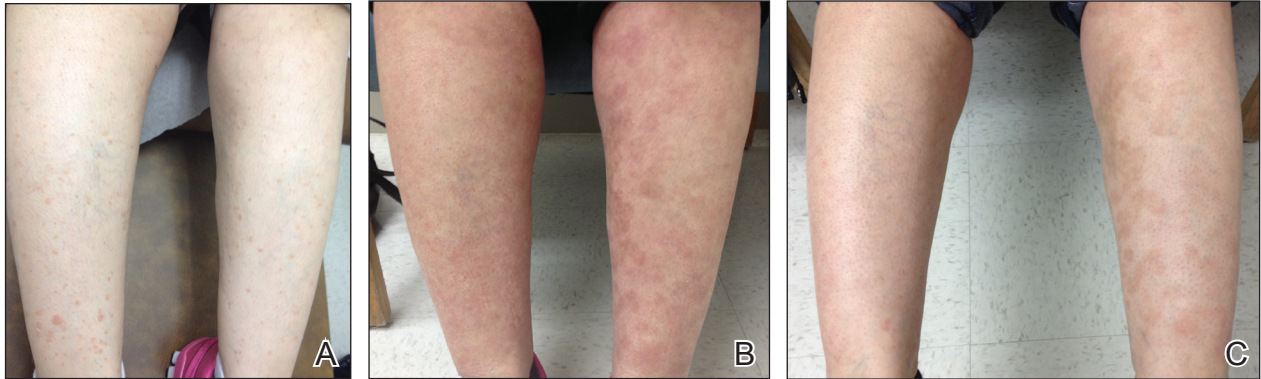
Postinflammatory hyperpigmentation is an acquired excess of pigment due to a prior disease process such as an infection, allergic reaction, trauma, inflammatory disease, or drug reaction. In our patient, this finding was unusual because tazarotene has been shown to be an effective treatment of PIH.^{2,3}

In PIH, there is either abnormal production or distribution of melanin pigment in the epidermis and/or dermis. Several mechanisms for PIH have been suggested. One potential mechanism is disruption of the basal cell layer due to dermal lymphocytic inflammation, causing melanin to be released and trapped by macrophages present in the dermal papillae. Another possible mechanism

From the Department of Dermatology, University of Texas Medical Branch at Galveston.

The authors report no conflict of interest.

Correspondence: Kristyna Gleghorn, MD, University of Texas Medical Branch at Galveston, 4.112 McCullough, 301 University Blvd, Galveston, TX 77555 (kglegho@utmb.edu).



A, On initial presentation, multiple, hyperpigmented, red-brown, 2- to 6-mm papules on the extensor surface of the legs and thighs were observed. B, After 9 weeks of treatment with 5-fluorouracil cream on the right leg and tazarotene cream 0.1% on the left leg, slight improvement was noted, but the lesions were still erythematous. C, After 14 weeks of treatment, there was complete resolution of lesions on both legs; however, postinflammatory hyperpigmentation was observed on the left leg, which had been treated with tazarotene.

is epidermal hypermelanosis, in which the release and oxidation of arachidonic acid to prostaglandins and leukotrienes alters immune cells and melanocytes, causing an increase in melanin and increased transfer of melanin to keratinocytes in the surrounding epidermis.⁴

Treatment of PIH can be a difficult and prolonged process, especially when a dermal rather than epidermal melanosis is observed. Topical retinoids, topical hydroquinone, azelaic acid, corticosteroids, tretinoin cream, glycolic acid, and trichloroacetic acid have been shown to be effective in treating epidermal PIH. Tazarotene is a synthetic retinoid that has been proven to be an effective treatment of PIH³; however, in our patient the PIH progressed with treatment. One plausible explanation is that irritation caused by the medication led to further PIH.^{2,5}

It is uncommon for tazarotene to cause PIH. Hyperpigmentation is listed as an adverse effect observed during the postmarketing experience according to one

manufacturer⁶ and the US Food and Drug Administration; however, details about prior incidents of hyperpigmentation have not been reported in the literature. Our case is unique because both treatments showed considerable improvement in HLP, but more PIH was observed on the tazarotene-treated leg.

REFERENCES

1. Bean SF. Hyperkeratosis lenticularis perstans. a clinical, histopathologic, and genetic study. *Arch Dermatol.* 1969;99:705-709.
2. Callender V, St. Surin-Lord S, Davis E, et al. Postinflammatory hyperpigmentation: etiologic and therapeutic considerations. *Am J Clin Dermatol.* 2011;12:87-99.
3. McEvoy G. Tazarotene (topical). In: *AHFS Drug Information.* Bethesda, MD: American Society of Health-System Pharmacists, Inc; 2014:84-92.
4. Lacz N, Vafaie J, Kihiczak N, et al. Postinflammatory hyperpigmentation: a common but troubling condition. *Int J Dermatol.* 2004;43:362-365.
5. Tazorac (tazarotene) cream [package insert]. Irvine, CA: Allergan, Inc; 2013.
6. Tazorac (tazarotene) gel [package insert]. Irvine, CA: Allergan, Inc; 2014.