

Case Report

Trifarotene triumph: a novel topical approach for progressive cribriform and zosteriform hyperpigmentation

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ABSTRACT

Progressive cribriform and zosteriform hyperpigmentation (PCZH) is an uncommon idiopathic dermatosis, typically presenting in adolescence as asymptomatic hyperpigmented lesions distributed along Blaschko's lines. Treatment options remain limited, with no standardized therapy established. A 21-year-old healthy female presented with a 1.5-year history of progressive, asymptomatic hyperpigmented patches involving the right torso, abdomen, lower limb, shoulder, and back. Histopathology confirmed PCZH, demonstrating epidermal hyperplasia, basal layer hyperpigmentation, and pigmentary incontinence. Owing to the patient's reluctance to undergo laser therapy, a conservative off-label regimen of topical trifarotene (50 µg/g) was initiated nightly. After six months, the patient achieved near-complete clearance of pigmentation with excellent tolerability. Trifarotene, a fourth-generation topical retinoid, exhibits high selectivity for retinoic acid receptor-γ (RAR-γ), the predominant isoform in epidermis. It enhances keratinocyte differentiation, regulates pigmentation, and modulates inflammatory pathways at lower doses with superior tolerability compared to earlier retinoids. Although primarily approved for acne, its pharmacological profile supports potential utility in pigmentary dermatoses such as PCZH. This case highlights the successful off-label use of trifarotene in PCZH, underscoring its promise as a novel therapeutic approach in idiopathic pigmentary disorders.

Keywords: Trifarotene, Novel approach, Progressive cribriform, Zosteriform hyperpigmentation

INTRODUCTION

Progressive cribriform and zosteriform hyperpigmentation (PCZH) is an uncommon idiopathic dermatosis typically presenting in late adolescence. The lesions are asymptomatic, reticulated, and arranged in a zosteriform pattern along Blaschko's lines, most often involving the trunk.¹⁻⁵ Histopathology reveals basal layer hyperpigmentation, epidermal hyperplasia, and pigmentary incontinence with dermal melanophages.^{5,6} PCZH must be differentiated from conditions with linear hyperpigmentation such as linear and whorled nevoid hypermelanosis (LWNH), Becker's nevus, incontinentia pigmenti (stage IV), and post-inflammatory

hyperpigmentation.⁶ Currently, there is no standardized therapy. Treatment options range from topical retinoids, corticosteroids, hydroquinone, and chemical peels to lasers (Q-switched Nd:YAG, fractional CO₂), but outcomes are variable and relapse is common.⁷ Trifarotene, a selective RAR-γ agonist, has shown promise in acne vulgaris and is now being explored in other dermatologic conditions.^{2,3}

CASE REPORT

A 21-year-old otherwise healthy female presented with a 1.5-year history of gradually progressive, black-colored patches distributed over the right side of the torso,

extending to the abdomen, lower limb, shoulder, and back. Lesions began on the flank and progressed linearly. She denied preceding trauma, inflammation, or topical applications. Hair, nails, and mucosal surfaces were unaffected. There was no significant medical or family history.

Dermatological examination revealed asymptomatic, reticulated, hyperpigmented patches in a zosteriform distribution (Figure 1A and C).



Figure 1: (A) Skin lesions before with pigmentation and (B) after treatment with resolution of pigmentation; (C) skin lesions before with pigmentation and (D) after treatment with resolution of pigmentation.

Histopathology of an abdominal lesion revealed epidermal hyperplasia with thickened and elongated rete ridges, basal layer hyperpigmentation, and dermal melanophages, consistent with pigmentary incontinence (Figure 2 and 3). Given reluctance to undergo laser treatment, an off-label trial of topical trifarotene 50 µg/g was initiated, applied nightly at three finger-tip units (FTU) per affected area. After six months of continuous therapy, remarkable improvement was observed with near-complete resolution of pigmentation on the chest, hand, and abdomen (Figure 1B and D). Tolerability was excellent, with no reported irritation or adverse effects.

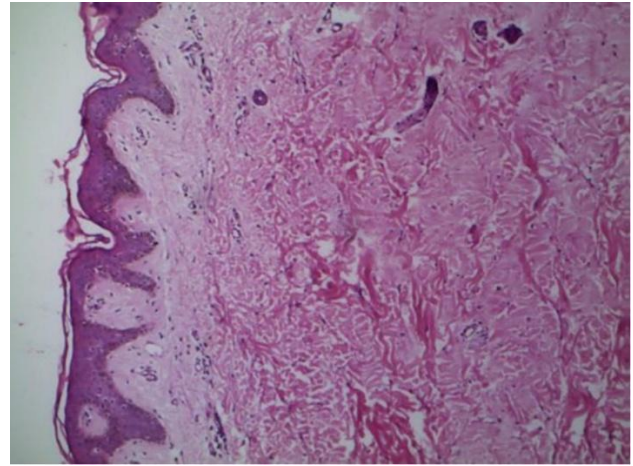


Figure 2: Epidermal hyperplasia with thickening and elongation of rete ridges.

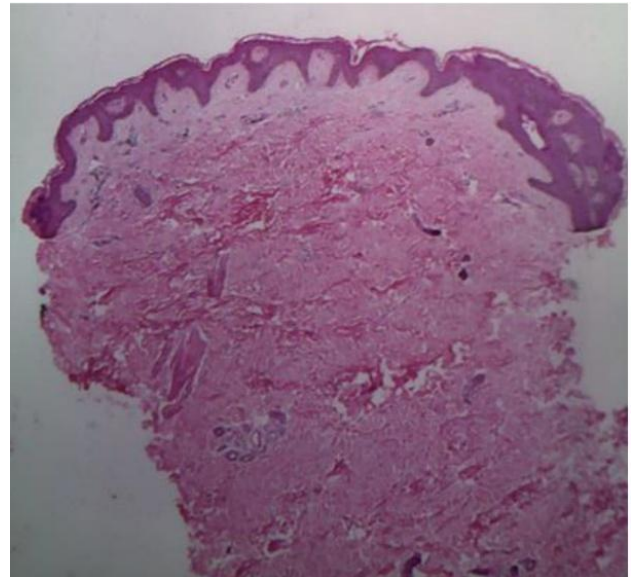


Figure 3: The basal layer shows increased melanin pigmentation; papillary dermis shows mild fibroplasia with irregular deposition of melanophages.

DISCUSSION

PCZH is considered a disorder of cutaneous mosaicism, reflecting postzygotic mutations leading to clone-specific skin manifestations along Blaschko's lines.⁵ The persistent hyperpigmentation is attributed to basal keratinocyte melanin retention and dermal pigmentary incontinence, with melanophages scattered in the papillary dermis.⁶

Traditional treatments

Topical depigmenting agents (hydroquinone, azelaic acid, kojic acid) have limited and inconsistent efficacy. Topical/systemic retinoids (tretinoin, adapalene, isotretinoin) improve pigmentation by increasing epidermal turnover and reducing melanosome transfer but

are often associated with irritation.^{7,8} Laser therapies (Q-switched ruby, Nd:YAG, CO₂) have been reported with partial clearance, though recurrence and post-inflammatory pigmentation are frequent concerns.⁷

Trifarotene advantages

Selective RAR- γ agonism, the dominant isoform in epidermis.^{1,2} Potent keratinocyte differentiation and reduced hyperproliferation. Anti-inflammatory effects via inhibition of AP-1 activity and leukocyte migration.^{3,4} Superior tolerability at lower doses compared with older retinoids.³ Potential to regulate melanogenesis through indirect modulation of melanocyte-keratinocyte interactions.

To date, there are no prior published reports of trifarotene use in PCZH. However, given its established role in truncal acne and emerging exploration in pigmentary disorders, our findings support expanding its indications.^{3,4,8,9}

Learning points

Progressive cribriform and zosteriform hyperpigmentation (PCZH) is a rare idiopathic pigmentary dermatosis, typically presenting along Blaschko's lines in young adults, and requires histopathology for confirmation.

Differential diagnosis includes linear and whorled nevoid hypermelanosis, incontinentia pigmenti (stage IV), Becker's nevus, and post-inflammatory hyperpigmentation.

Conventional therapies (depigmenting agents, older retinoids, and lasers) often yield suboptimal or inconsistent results, with recurrence or adverse effects.

Trifarotene, a fourth-generation RAR- γ selective retinoid, demonstrated excellent efficacy and tolerability in this PCZH case, achieving near-complete clearance in six months.

This is among the first reported cases of successful off-label use of trifarotene in PCZH, highlighting its therapeutic potential for pigmentary dermatoses and underscoring the need for controlled studies.

CONCLUSION

This case demonstrates the first documented off-label use of trifarotene in PCZH, with remarkable clinical improvement and excellent tolerability. Trifarotene's unique pharmacological profile—selective RAR- γ activation, modulation of epidermal turnover, and indirect regulation of pigmentation—makes it a promising therapeutic option for idiopathic pigmentary dermatoses where conventional agents or lasers are suboptimal.

While single case reports cannot establish efficacy, they provide a foundation for prospective studies and controlled trials to evaluate trifarotene's role in pigmentary conditions such as PCZH, LWNH, and post-inflammatory hyperpigmentation. Given its safety, accessibility, and tolerability, trifarotene may emerge as a valuable addition to the therapeutic armamentarium for pigmentary dermatoses.

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REFERENCES

1. Aubert J, Piwnica D, Bertino B, Bolduc C, Nieloud C, Aubert C, et al. Nonclinical and human pharmacology of the potent and selective topical retinoic acid receptor- γ agonist trifarotene. *Br J Dermatol.* 2018;179(2):442-56.
2. Thoreau E, Arlabosse JM, Bouix-Peter C, Paccalet A, Corbier C, Moulin A, et al. Structure-based design of trifarotene (CD5789), a potent and selective RAR γ agonist for the treatment of acne. *Bioorg Med Chem Lett.* 2018;28(10):1736-41.
3. Tan J, Chavda R, Baldwin H, Dreno B. Management of acne vulgaris with trifarotene. *J Cutan Med Surg.* 2023;27(4):368-74.
4. Cosio T, Di Prete M, Gaziano R, Lanna C, Orlandi A, Di Francesco P, et al. Trifarotene: a current review and perspectives in dermatology. *Biomedicines.* 2021;9(3):237.
5. Rower JM, Carr RD, Lowney ED. Progressive cribriform and zosteriform hyperpigmentation. *Arch Dermatol.* 1978;114(1):98-9.
6. Bologna JL, Orlow SJ, Glick SA. Lines of Blaschko. *J Am Acad Dermatol.* 1994;31(2 Pt 1):157-90.
7. Omi T, Yamashita R, Kawana S, Sato S, Naito Z. Low Fluence Q-Switched Nd: YAG Laser Toning and Q-Switched Ruby Laser in the Treatment of Melasma: A Comparative Split-Face Ultrastructural Study. *Laser Ther.* 2012;21(1):15-4.
8. Kang HY, Ortonne JP. What should be considered in treatment of melasma. *Ann Dermatol.* 2010;22(4):373-378.
9. Piccolo D, Fusco I, Crisman G, Zingoni T, Conforti C. Efficacy and Safety of Q-Switched 1064/532 nm Nd:YAG Lasers on Benign Hypermelanosis in Dark-Skinned Individuals—A Preliminary Study. *J Clin Med.* 2024;13:1615.

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