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Successful Treatment of Extensive Verrucous Epidermal Nevus with Combination Oral Acitretin and Topical 30% Urea Cream: A Literature Review & Case Report Study

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Abstract

Epidermal nevi (EN) are hamartomas that are characterized by hyperplasia of the epidermis and adnexal structures. This case report describes the successful treatment of extensive, long-standing Verrucous Epidermal Nevus (VEN) in a 15-year-old female using a combination oral Acitretin (25mg/day) and topical 30% Urea cream applied nightly. After failure of multiple prior therapies including topical agents and ablative CO2 laser, this regimen achieved a dramatic clinical and cosmetic response within 60 days, resulting in complete resolution of lesions with only mild cheilitis as a side effect.
Laboratory monitoring remained normal throughout treatment. This combination offers a promising non-surgical approach for extensive VEN.

Keywords: Verrucous Epidermal Nevus, Acitretin, Urea Cream.

Introduction

Epidermal nevi (EN) are hamartomas that are characterized by hyperplasia of the epidermis and adnexal structures. Lesions with prominent adnexal components (sebaceous, follicular, and/or apocrine) are sometimes referred to as “organoid”, while lesions with primarily epidermal differentiation are known as “non-organoid” or “keratinolytic” nevi (1).

Although topical therapies appear to be unsuccessful and recurrences are frequent, physical therapy techniques have been employed (2). Although it can occur anywhere, it is less frequent on the head and neck, infrequent on the face, and extremely uncommon to affect the oral mucosa (3). Most of these nevi occur sporadically, with a few cases in families. Sixty percent of EN occur at birth, while 95% of cases are present by age 7 years. Variants of epidermal nevi include verrucous epidermal nevus (VEN), nevus sebaceous, nevus comedonicus and eccrine nevus (4,5).

Case Presentation:

A healthy 15-year-old unmarried girl attended the dermatological outpatient clinic of Al-Kindy Teaching Hospital in Baghdad-Iraq in MAY 2024 with extensive VEN involving her trunk, upper limbs, and lower limbs. The lesions were first noted at birth as asymptomatic, tiny, skin-colored, verrucous papules on the trunk.

Over time, the papules progressively coalesced into widespread, dark brown, serpiginous plaques with a markedly verrucous and rough surface texture.

The diagnosis was confirmed clinically based on history and clinical examination aided by dermoscopic examination which revealed typical features of VEN (large brown circles and cerebriform pattern) (figure 3). She had no history of seizures, learning disabilities, hearing impairments, or any other underlying diseases, and her growth and developmental history were otherwise normal. No other family members have the same issue. the patient had a history of multiple failed treatments, including various topical therapies and ablative CO2 laser, providing no significant benefit.

Therapeutic Intervention:

A comprehensive evaluation was conducted to exclude contraindications (e.g., pregnancy, severe hepatic/renal impairment, hyperlipidemia), The patient was informed about all possible side effects, with emphasis on the importance of avoiding pregnancy for at least 3 years after stopping acitretin.

A combination therapy was initiated:

- Oral Acitretin: 25 mg once daily, taken with a fatty meal to enhance absorption.
- Topical 30% Urea Cream: Applied liberally to all affected areas once nightly to leverage its keratolytic and moisturizing properties.

Pretreatment and Monitoring:

Baseline laboratory investigations (Complete Blood Count - CBC, Lipid Profile, Liver Function Tests - LFTs) were performed. These tests were repeated on day 30 and day 60 of treatment.

The patient was followed up monthly to assess clinical response, side effects, and treatment compliance.

Clinical Response:

- Day 30: Significant improvement was already evident, in the form of a reduction in both the size and thickness of the verrucous plaques.
- Day 60: A dramatic clinical and cosmetic response was observed. All lesions showed complete resolution (Figs 1B, 2B - referenced in the original document).

Side Effects: The only reported side effect was mild cheilitis, a known adverse effect of systemic retinoid.

Compliance: The patient demonstrated excellent compliance with the prescribed regimen.

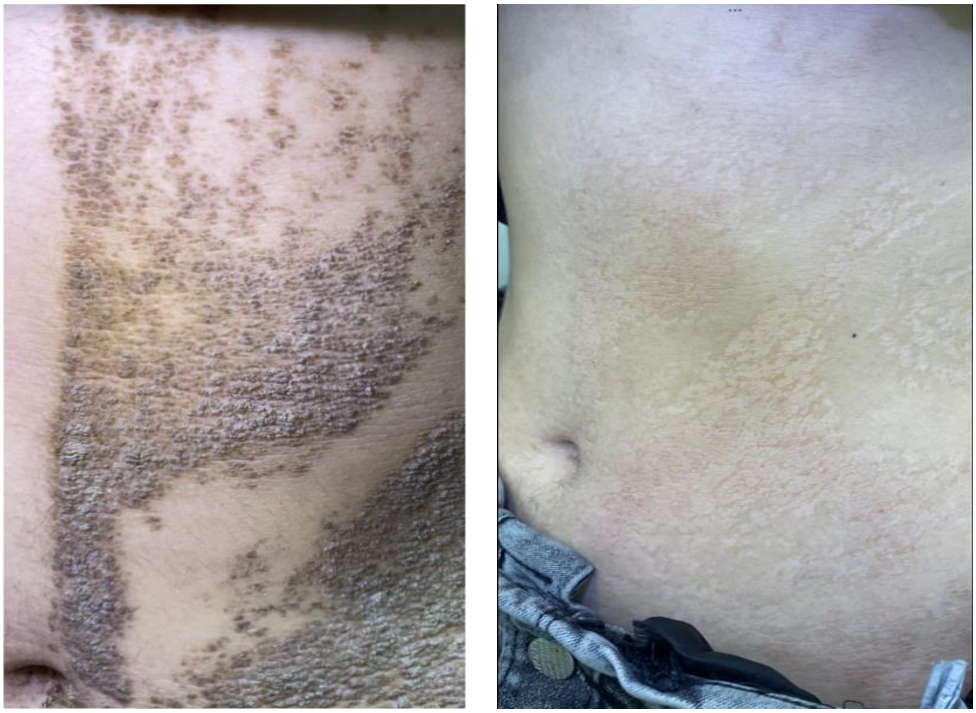

Fig 1. A widespread brown colored verrucous plaque on the trunk. B, After 60days of treatment, the cosmetic and clinical response was excellent.

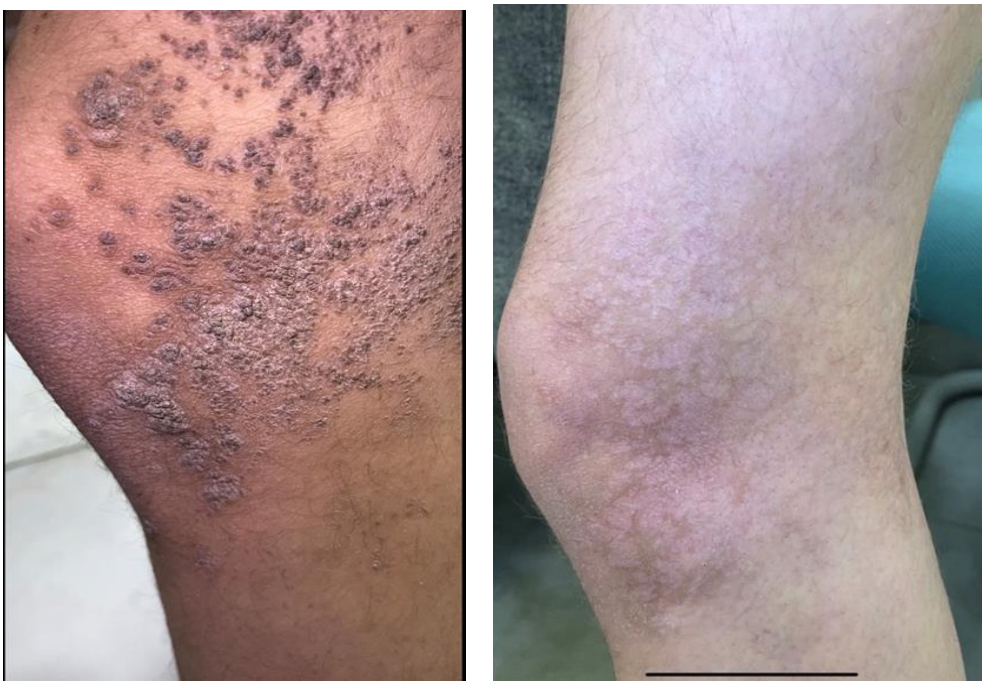

Fig 2. A clinical image of epidermal nevus lesion on the left leg. B, Dramatic response after 60 day of treatment with complete clearance of lesions

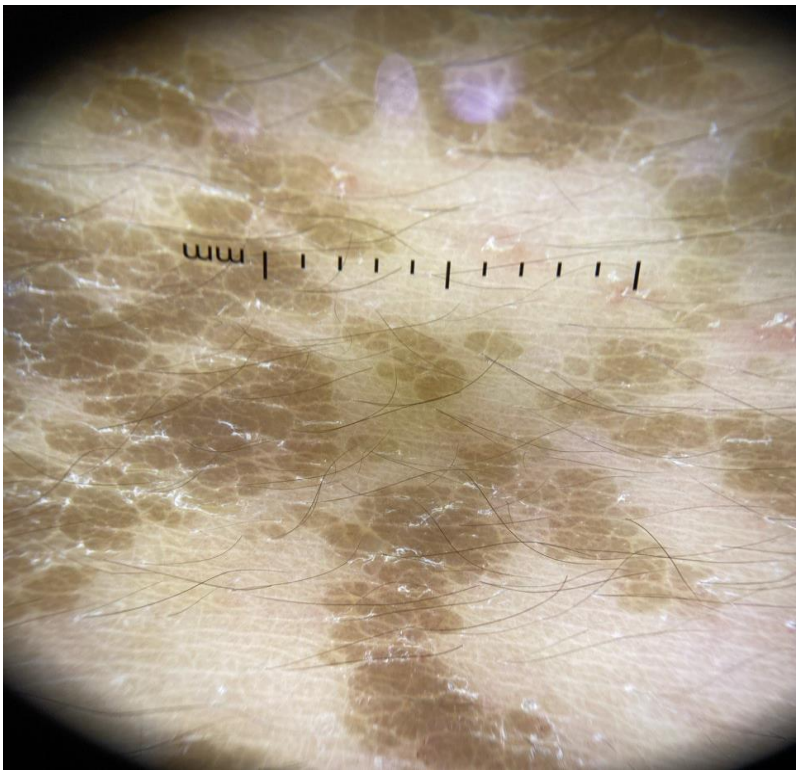

Fig.3 a dermoscopy image of the lesion which shows features of VEN: large brown circles and cerebriform pattern.

Table 1: The previously reported epidermal nevus lesions treated with systemic retinoids and their affected site.

Author	**Age and sex**	**Site of VEN**	**Treatment and outcome**
Abdel-Aal (1983)	57 y/M	Hands, feet, face, trunk, right temple	Oral etretinate 25 mg three times a day resulted in improvement in a month and complete regression in 80 days
Happle et al. (1977)	--	Systematized VEN	Oral etretinate caused marked improvement in VEN
Tas¸kapan et al. (1998)	20Y/M	Right side of trunk, buttocks and thighs	Oral acitretin 75 mg/day improved the lesions at 3 weeks. The dose was discontinued at 3 months. Lesions relapsed 6 weeks after discontinuation
Geetika Chhabra, Prashant Verma and Shruti Sharma. (2019)	15Y/M	the left side of trunk and lower limb	A 10 mg dose of acitretin per day for 2 months. The lesions had regressed significantly leaving behind some hyperpigmentation

Discussion

Epidermal nevi are a cutaneous hamartoma with several clinical variations, including a verrucous form. Hyperplasia of the epidermis is the hallmark of a VEN, which usually manifests as skin-colored to brown, well-defined papillomatous plaques or verrucous papules.
These tumors may be seen in the head, trunk, or extremities, among other sites (6).
These lesions in the current case appeared on an extended area of the body since birth leading to cosmetic problems associated with anxiety and fear of bullying at school with our society expectations regarding young teenage female the distribution in our case was similar to that of 14 year old Thai boy reported by Chanasumon et al that also presented with multiple asymptomatic hyperkeratotic brownish plaques on face, trunk, and extremities his lesions first appeared since he was born, becoming thicker and larger over time. Nothing significant regarding his growth and developmental history. He had never experienced seizures, learning disabilities, hearing loss, or visual changes. He denied having family members with similar findings all these points are similar to our case (7). Manoharan Ramalingam 2 and Manoharan Dhanaraj 1 also reported another case, A 20-year-old woman with nonconsanguineous parents presented with complaints of elevated skin sores throughout her body from infancy. Age-related thickening and darkening of the lesions was a history. There was no history of seizures, learning disabilities, vision changes, or hearing impairments, and the growth and developmental histories were normal, just like in our patient (8).
A VEN usually has many different treatment modalities with poor or unreliable response and long course of treatment (9,10). surgical excision is one of many options for epidermal nevi but might not be possible when a skin lesion is so wide spread as our case, and it might cause scarring (11). In this case, the patient was against surgical excision because of concerns of postoperative scarring as in the case reported by Lee BJ, Mancini AJ, Renucci J, Paller AS, Bauer BS where the authors report 4 patients with extensive ILVEN treated successfully with full-thickness surgical excision while they did achieve complete obliteration of the nevi, and no recurrence but all comes at the cost of obligatory scar formation. (12)
Acitretin: A systemic retinoid that normalizes keratinocyte differentiation and proliferation, targeting the underlying pathological clone of cells. Its anti-keratinizing and anti-proliferative effects are crucial for reducing the bulk and verrucous nature of the nevus. (13)
The use of acitretin in the treatment of VEN was reported by Geetika Chhabra, Prashant Verma, Shruti Sharma, where also a 15-year-old boy was started on acitretin with no topical treatment. Following a daily dose of 10 mg, the lesions started to heal after three weeks and had significantly disappeared by the end of two months, leaving a little hyperpigmentation (14). where in our case there was the addition of topical agent (urea 30%) with similar duration of treatment of acitretin at a dose of 25 mg with complete resolution of the lesions and with a residual hypopigmentation which was acceptable by the patient.
Higher amounts of urea can denature proteins like keratin by causing conformational changes in their protein structure or by rupturing their hydrogen bonds (15),(16). providing a potent

keratolytic and humectant action, softens the rough texture of the skin, and improves skin hydration. The use of urea cream in treating epidermal nevi was tried previously by J. K. Hong, H.S.Han and K.H.Yoo where 20% urea cream was used as a treatment combined with topical corticosteroid, topical calcipotriol as a triple combination as a sole treatment for a localized lesion of ILVEN used as a 'penetration enhancer' to optimize the effects of drugs. (17)
In our case urea was added as an additional topical treatment for its keratolytic properties specially at a concentration of 30%.
This case demonstrates the remarkable efficacy and safety of combining low-dose oral Acitretin with topical 30% Urea cream for treating extensive, recalcitrant VEN. The success likely stems from the synergistic mechanisms.
The patient was followed up for 12 months after discontinuing treatment with no signs of relapse. The rapid and complete response within 60 days, especially after the failure of multiple other interventions including CO2 laser, highlights the potential of this specific combination. The use of a relatively low dose of Acitretin (25mg/day) contributed to the favorable safety profile, with only mild cheilitis observed and no laboratory abnormalities. Strict laboratory monitoring and pregnancy prevention counseling (critical for Acitretin) are essential components of this treatment approach.

Conclusion:

The combination of low-dose oral Acitretin (25mg/day) and nightly topical 30% Urea cream proved to be a highly effective, well-tolerated, and non-invasive treatment for extensive Verrucous Epidermal Nevus in this adolescent patient, achieving complete clearance within 60 days. This regimen represents a valuable therapeutic option for patients with widespread or refractory VEN, offering significant cosmetic and clinical improvement where other modalities have failed. Additional research is necessary to evaluate long-term remission and validate these results in larger patient groups.

Ethics Approval and Consent to Participate

The study received ethical approval from Alkindy Medical College, University of Baghdad (Document No. 204, dated April 29, 2024). Written informed consent was obtained from the patient, and confidentiality with secure handling of patient information was maintained throughout all study time.

Conflict of Interest: Non

Funding: Nil

References:

1. Solomon LM, Esterly NB. Epidermal and other congenital organoid nevi. *Current problems in pediatrics*. 1975 Jan 1;6(1):3-56.
2. Elisabet P, Fernando G, AgustÍ T, Immaculada G, JÚLIA SS, Ramon P. Inflammatory linear verrucous epidermal nevus successfully treated with methyl-aminolevulinate photodynamic therapy. *Dermatologic surgery*. 2010 Feb 1;36(2):253-6.
3. Özçelik D, Parlak AH, Öztürk A, Kavak A, Çelikel N. Unilateral linear verrucous epidermal nevus of the face and the oral mucosa. *Plastic and reconstructive surgery*. 2005 Feb 1;115(2):17e-9e.

4. Wolff K, Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffell DJ. In: Fitzpatrick's Dermatology in general medicine. 5th ed. Vol. 1. New York: McGraw Hill, Inc; 1999. *Epidermal nevus*; pp. 876–8.
5. Waltz KM, Helm KF, Billingsley EM. The spectrum of epidermal nevi: a case of verrucous epidermal nevus contiguous with nevus sebaceus. *Pediatric dermatology*. 1999 May;16(3):211-3.
6. Ho, V.C.Y. Benign epithelial tumors Freedberg, I.M. · Eizen, A.Z. · Wolff, K. (Editors) Fitzpatrick's dermatology in general medicine McGraw-Hill, New York, 1999; 873-890
7. Chanasumon N, Chayavichitsilp P. Systematized epidermal nevus: A rare case report and a review of literature. *Thai Journal of Dermatology*. 2016 Jul 1;32(3):212-6.
8. Dhanaraj M, Ramalingam M. Systematised epidermal nevus-a case report. *Journal of Clinical and Diagnostic Research*: *JCDR*. 2015 Feb 1;9(2):WD01.
9. Fox BJ, Lapins NA. Comparison of treatment modalities for epidermal nevus: a case report and review. *Dermatologic Surgery*. 1983 Nov 1;9(11):879-85.
10. Baba T, Narumi H, Hanada K, Hashimoto I. Successful treatment of dark-colored epidermal nevus with ruby laser. *The Journal of Dermatology*. 1995 Aug;22(8):567-70.
11. Dellon AL, Luethke R, Wong L, Barnett N. Epidermal nevus: surgical treatment by partial-thickness skin excision. *Annals of plastic surgery*. 1992 Mar 1;28(3):292-6.
12. Lee BJ, Mancini AJ, Renucci J, Paller AS, Bauer BS. Full-thickness surgical excision for the treatment of inflammatory linear verrucous epidermal nevus. *Annals of plastic surgery*. 2001 Sep 1;47(3):285-92.
13. Brun PJ, Yang KJ, Lee SA, Yuen JJ, Blaner WS. Retinoids: Potent regulators of metabolism. *Biofactors.* 2013 Mar;39(2):151-63.
14. Chhabra G, Verma P, Sharma S. A case of systematized verrucous epidermal nevus successfully treated with low dose acitretin. *Dermatologic Therapy*. 2019 Nov 1;32(6).
15. Celleno L. Topical urea in skincare: a review. *Dermatologic therapy*. 2018 Nov;31(6):e12690.
16. Pan M, Heinecke G, Bernardo S, Tsui C, Levitt J. Urea: a comprehensive review of the clinical literature. *Dermatology online journal.* 2013;19(11).
17. Hong JK, Han HS, Yoo KH. Inflammatory linear verrucous epidermal naevus successfully treated with a combination of triple topical agents (corticosteroid, calcipotriol and 20% urea). *Clinical and experimental dermatology*. 2021 Jul 1;46(5):940-2.