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Clinical Medicine Insights: Dermatology

Successful Treatment with Calcipotriol for Nevoid Hyperkeratosis of the Nipples

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ABSTRACT: Nevoid hyperkeratosis of the breast is a rare condition affecting the nipple, the areola, or both. Different therapeutic options have been used with varying results, but there is no uniformly effective treatment. We report a case of nevoid hyperkeratosis of the nipple in a woman presenting with thickening and hyperpigmentation of both nipples for 15 years. Histologic examination confirmed the diagnosis of nevoid hyperkeratosis. The patient was successfully managed by topical calcipotriol. Calcipotriol is an effective therapeutic option in nevoid hyperkeratosis of the nipple and shows rapid outcome.

KEYWORDS: nipple, breast, nevoid hyperkeratosis, calcipotriol

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Introduction

A 25-year-old woman had seen her gynecologist for hyperkeratotic lesions on both nipples. The lesions first appeared at the age of 8 years. This symptom was associated with an intermittent thick yellowish flow without any pain or pruritus. Otherwise, the patient was healthy and took no regular medications. Upon dermatologic consultation, we found an irregular keratotic thickening of both nipples with a verrucous surface, which was more marked on the left side (Fig. 1). The pressure of the nipples showed no serosity. Clinical examination of the breasts and axillary lymph nodes was normal. In addition, we noted retentional acne and a mild hirsutism. Breast ultrasound was normal. Routine laboratory tests were within normal limits. Biopsy showed orthokeratotic hyperkeratosis, moderate acanthosis, papillomatosis, and a dermal perivascular lymphocytic infiltrate (Fig. 2), confirming the diagnosis of nevoid hyperkeratosis of the nipple. The patient had taken calcipotriol ointment 3% twice per day. Remarkable improvement was observed within the third week. The patient had no side effects after applying the medication. The treatment was stopped three months later (Fig. 3), without any recurrence at the one-year follow-up visit.

Discussion

Hyperkeratosis of the nipple and areola (HNA) was first described by Tauber in 1923. In 1938, Levy-Frankel classified HNA as having three distinct types: HNA that presents as an extension of an epidermal nevus, HNA associated with other dermatoses (ichthyosis, ichthyosiform erythroderma, acanthosis nigricans, T-cell lymphoma, Darier's disease, eczema, etc), and idiopathic HNA, also known as nevoid HNA (NHNA).[1]

NHNA is a rare condition of unknown etiology; thus far, fewer than 100 cases have been reported.[2] The lesions are benign and asymptomatic, but may have consequences of functional, aesthetic, and psychological in nature. Eighty percent of cases occur in women and are often manifested during puberty or pregnancy.[2,3] The disease may also occur

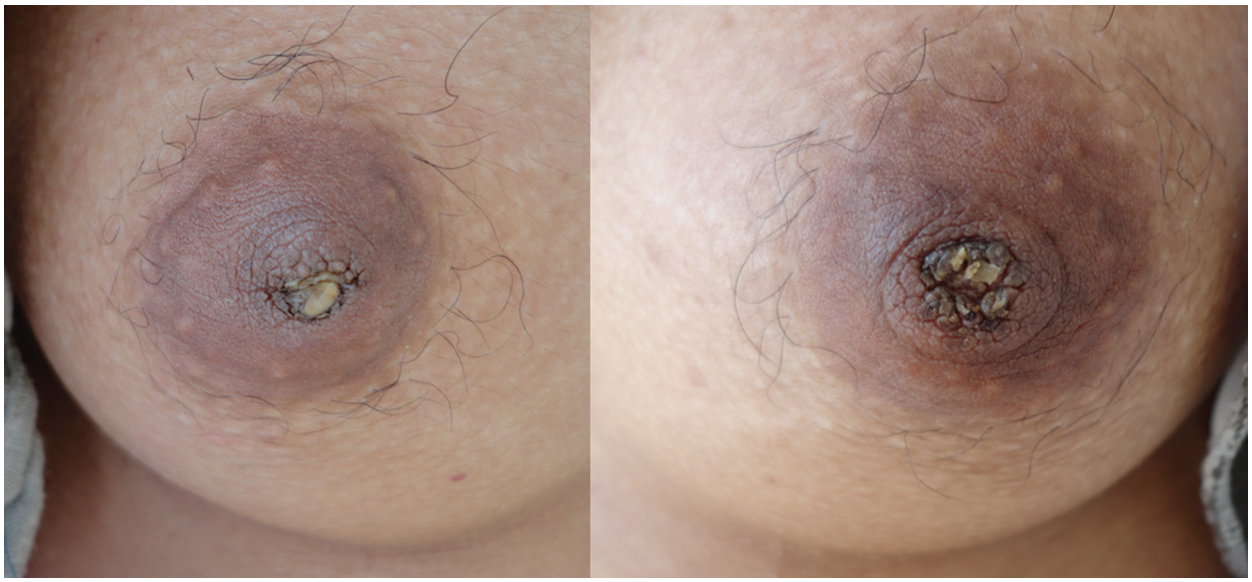

Figure 1. Bilateral involvement of the nipple.

in men receiving hormonal therapy, but is also found out of this context.[2] The distribution is typically bilateral, but can be unilateral.[4] NHNA is clinically characterized by verrucous thickening and pigmentation of the nipple and/or areola.[4] Diagnosis is confirmed by histology; the main features include hyperkeratosis, acanthosis, and papillomatosis, which closely mimics symptoms of epidermal nevus or acanthosis nigricans.[4] Differential diagnoses include Paget's disease, superficial basal cell carcinoma, dermatophytosis, seborrheic keratosis, and Bowen disease.[4] Warty changes of areolas and nipples may also be observed in mycosis fungoides and follicular mucinosis.[5] Histologically, NHNA can also be misinterpreted as mycosis fungoides.[6] In our case, semiology, bilateral, and non-progressive localization over several years

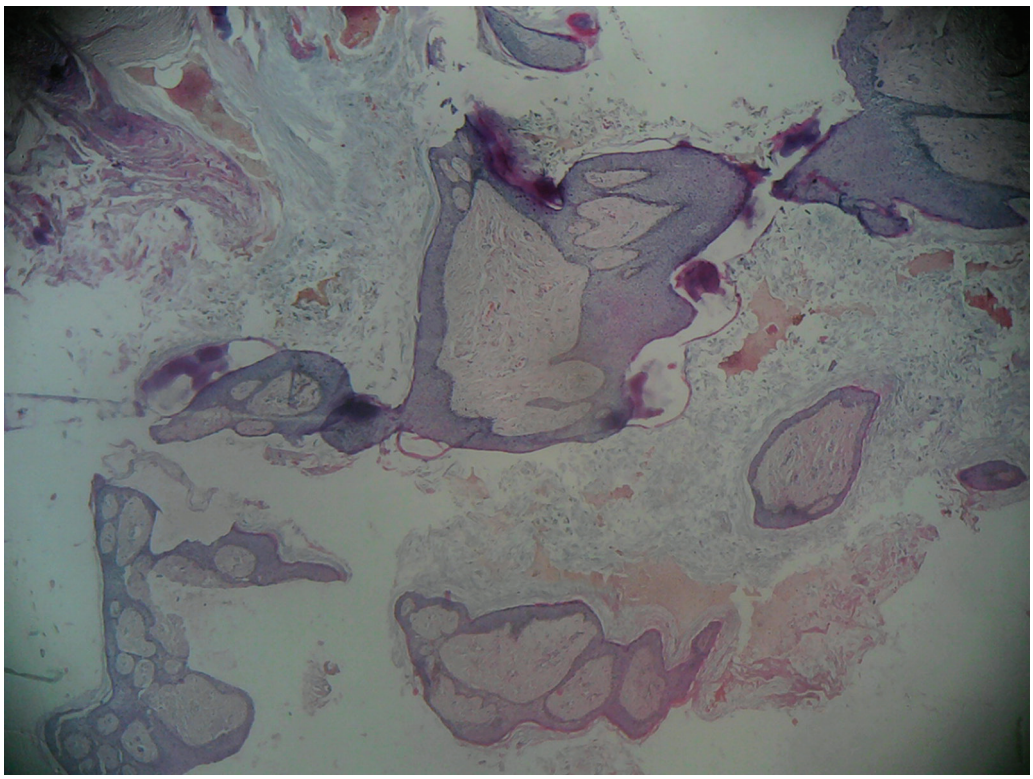

Figure 2. Histopathology shows hyperkeratosis and irregular acanthosis and papillomatosis (Hematoxylin-eosin stain; original magnification × 40).

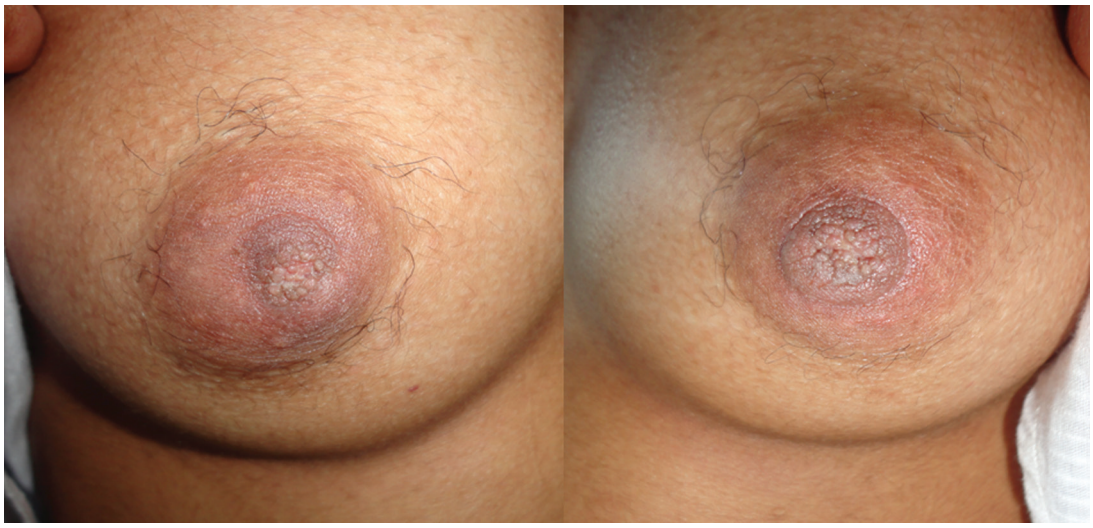

Figure 3. Outcome after three months.

allowed us to clinically rule out tumoral pathology, which was confirmed by histological findings. The aesthetic discomfort typically justifies therapeutic management in young patients. The prognosis is good, but without therapy, the lesions persist indefinitely.

There is no uniformly effective treatment for NHNA. Keratolytic agents such as salicylic 6%, retinoic and lactic acid 12%, and topical corticosteroids have been used with varying success in case reports.[7]

Cryotherapy, surgical ablation, or with radio frequency or a carbon dioxide laser excision can be considered if the patient is greatly disturbed by the cosmetic appearance and expects an immediate result.[8–10]

The lack of large series and prospective studies does not allow assessing the efficacy of different treatments. In a recently reported study of 25 pregnancy-associated nipple hyperkeratosis cases, 16 patients received a treatment.[11] Only curettage showed a complete response in one case. *N*-Petrolatum- and lanolin-based emollients were ineffective or only mildly effective and low potency topical steroids were mildly effective. A 12% ammonium lactate cream and a 12% lactic acid lotion were moderately effective. Two patients used a 0.025% tretinoin cream with mild or moderate improvement. Calcipotriol was not used but was mentioned as a therapeutic option.

Because of the localized nature of the lesions, we opted for non-ablative treatment. Topical calcipotriol has been used since 2002[12] in a few cases of NHNA, alone or combination with low-dose acitretin, with complete disappearance of the lesions in 3 to 6 months.[2,3,13,14] Its mechanism of action in HNA may rely on its effects on keratinocyte differentiation and proliferation.

This is the second case reported in a Moroccan woman.[14] Notably, our patient showed a dramatic improvement after only three weeks of treatment. When compared with the other treatment modalities, topical calcipotriol is safe, inexpensive, and effective with minimal side effects.

Author Contributions

Analyzed the data: WR, FE, LB, AB. Wrote the first draft of the manuscript: WR. Contributed to the writing of the manuscript: FE, LB, AB, KS, BH. Agree with manuscript results and conclusions: WR, FE, LB, AB, KS, BH. Jointly developed the structure and argument the paper: WR, FE, LB. Made critical revision approved final version: WR, FE, LB, AB, KS, BH. All authors reviewed and approved of the final manuscript.

DISCLOSURES AND ETHICS

As a requirement of publication the authors have provided signed confirmation of their compliance with ethical and legal obligations including but not limited to compliance with ICMJE authorship and competing interests guidelines, that the article is neither under consideration for publication nor published elsewhere, of their compliance with legal and ethical guidelines concerning human and animal research participants (if applicable), and that permission has been obtained for reproduction of any copyrighted material. This article was subject to blind, independent, expert peer review. The reviewers reported no competing interests.

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