Case Report

# Unilateral Nevoid Hyperkeratosis of Nipple and Areola in a Filipino Woman: A Case Report and Literature Review

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## Abstract

Nevoid hyperkeratosis of the nipple and areola (NHNA) is a rare, asymptomatic skin condition characterized by verrucous, hyperpigmented papules, and plaques. It predominantly affects the nipple and areola, often bilaterally. Less than 50 cases have been reported worldwide, with only 39% showing unilateral breast involvement. In the Philippines, a single medical literature from 2014 describes two cases of adolescent-onset NHNA. We report a rare case of a 40-year-old, Filipino woman with a 1-year history of a mildly pruritic, solitary, well-demarcated, irregularly shaped, black papule that progressed into a plaque on her right areola. There was suspicion of cutaneous malignancy due to some of the clinical features of the lesion and lack of response to initial treatment. With a correlation between clinical presentation and histopathologic findings, the features were consistent with NHNA. This is a benign skin condition that can mimic and must be differentiated from malignant tumors. Various treatment modalities were described in different medical literatures, some resulting in recurrence or treatment failure, but there is no standard management for this condition. Skin biopsy is crucial to rule out malignancy in cases presenting with persistent and progressively solitary pigmented lesions that do not respond to topical medications. The usual treatment options based on literature include various topicals, lasers, and surgical procedures. In our case, clobetasol propionate ointment was used. While most published cases show varied responses to topical corticosteroids, the result in our case was significant.

**Keywords:** Areola, case report, clobetasol propionate, nevoid hyperkeratosis, nipple

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## Introduction

In the year 1923, Tauber described a rare, idiopathic, and benign skin condition termed nevoid hyperkeratosis of the nipple and areola (NHNA).[1] It presents as asymptomatic, verrucous, hyperpigmented papules and plaques which are often bilateral and usually confined to the nipple, areola, or both. Hormonal influence may play a role in its pathogenesis as this skin condition commonly arises in women in their second or third decade in conjunction with the onset of puberty and pregnancy, respectively.[2] Patients with NHNA seek medical attention as it has a seemingly malignant appearance.[3]

A thorough literature review of published cases of NHNA was done, and their similarities and differences were compared to our case. This aims to contribute to the current limited information about the condition.

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## Case Report

A 40-year-old, married, Filipino, female housewife presented with a solitary, irregularly shaped, black plaque on her right areola. It started 1 year before consultation as a solitary hyperpigmented papule that gradually increased in size and in thickness which eventually progressed into a plaque. There was occasional mild pruritus with no pain or tenderness. There was no history of trauma, radiation treatment, surgery, or skin lesions before its appearance. There was no associated swelling, ulceration, discharge, or dimpling of the breast. The appearance of the lesion and the presence of pruritus were not related to her menstrual cycle. The patient did not complain of fever, joint pains, fatigue, or weight loss. She applied betamethasone dipropionate plus mupirocin ointment intermittently for 1 week with no improvement.

Three months before consultation, she had nummular dermatitis on the lateral side of her right breast sparing the nipple and areola that improved after the application of betamethasone dipropionate plus mupirocin ointment intermittently for 1 week. The patient was fit and in good general health with no known comorbidities. The patient's personal and family history was negative for warts, epidermal nevi, acanthosis nigricans, ichthyosis, atopy, endocrinopathies, psoriasis, lymphomas, skin cancer, or other types of cancer. She was a nonsmoker and nonalcoholic beverage drinker. The patient denied intake of herbal and dietary supplements or any other medications. She was a gravida 1, para 1, and delivered through normal spontaneous delivery in 2005. She has been taking oral contraceptive pills since her last pregnancy.

Cutaneous examination revealed a solitary, well-demarcated, irregularly-shaped, black plaque, some areas topped with white scales on the lateral aspect of her right areola that measured 3.5 cm × 2 cm in widest diameter [Figure 1a]. There was a solitary, well-defined, round, brown patch located on the lateral aspect of the right breast that measured 2 cm × 2 cm. On palpation, the right breast had no palpable mass, was not warm to touch, nontender, and nonindurated. There was no skin dimpling, nipple retraction, discharge, ulceration, or axillary lymphadenopathy. The right nipple was spared and the left breast had no lesions.

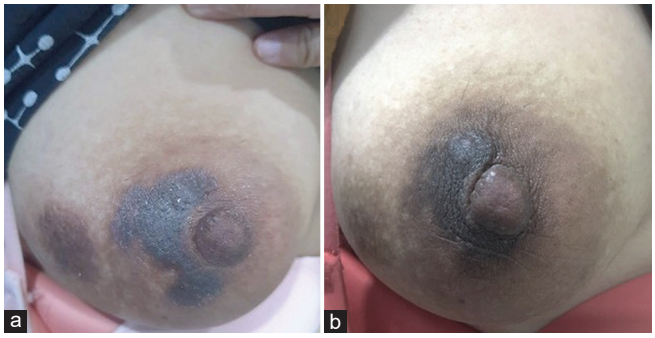


**Figure 1:** (a) Solitary, well-demarcated, irregularly shaped, black plaque on the lateral aspect of the right areola. (b) Three months after treatment with twice daily application of clobetasol propionate 0.05% ointment for 2 weeks showing a significant decrease in size and pigmentation of the plaque on the right areola

Histopathological examination [Figure 2a] revealed epidermis with marked acanthosis, marked basal layer hyperpigmentation, and squared rete ridges. There was minimal hyperkeratosis, parakeratosis, slight papillomatosis, and mild spongiosis [Figure 2b]. There were clumps of melanin in the keratinocytes at the spinous layer of the epidermis [Figure 2c]. There was a thick papillary dermis with fibroplasia and a dense superficial perivascular infiltrate of lymphohistiocytes with melanin granules and melanophages [Figure 2d]. A diagnosis of NHNA was made, and she was treated with twice daily application of clobetasol propionate 0.05% ointment for 2 weeks with significant improvement of the hyperpigmented plaque [Figure 1b] with resolution of pruritus on follow-up. The residual hyperpigmentation was then treated with once-daily application of a compounded mixture of tretinoin 0.05%, hydroquinone 4%, and triamcinolone 0.025% cream.

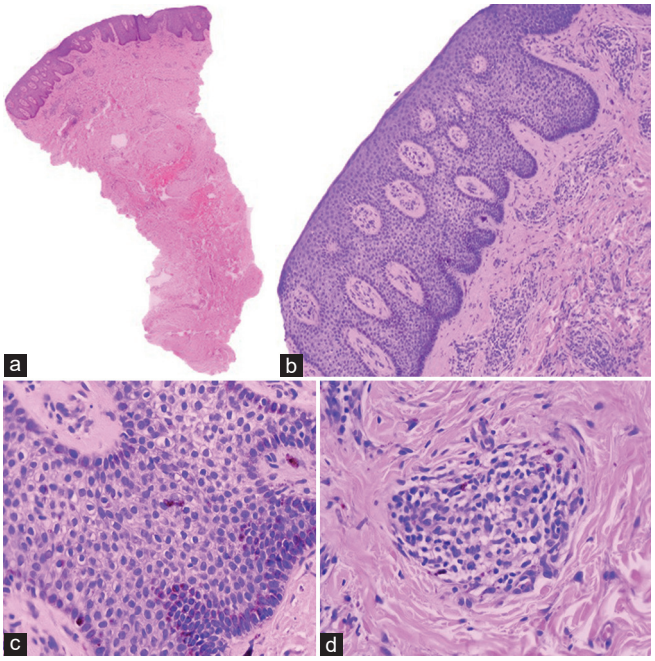


**Figure 2:** Biopsy of solitary plaque on the right areola on hematoxylin and eosin stain. (a) Epidermis with marked acanthosis, marked basal layer hyperpigmentation, slight papillomatosis, and squared rete ridges (×4). (b) Minimal hyperkeratosis, parakeratosis, and mild spongiosis (×10). (c) Clumps of melanin were seen in the keratinocytes at the spinous layer of the epidermis (×40). (d) Dense superficial perivascular infiltrate of lymphohistiocytes with melanin granules and melanophages in the dermis (×40)

## Discussion

NHNA is a rare, benign, and idiopathic skin condition described as slowly growing, verrucous, hyperpigmented papules and plaques affecting the nipple, areola, or both.[1] Hyperkeratosis of the nipple and areola is subdivided into three categories by Levy-Frenckel in 1938.[1] The first type is associated with epidermal nevus that occurs unilaterally and may be seen in both sexes.[4] On the other hand, several dermatoses such as acanthosis nigricans, Darier disease, chronic eczema, and cutaneous T-cell lymphoma are related to the second type.[5] This may affect both sexes, predominantly noted in women, and involves bilateral nipple and areola.[2] The third type has a nevoid form occurring bilaterally and idiopathically in women in their second or third decade.[2] Various literatures describe the hyperkeratosis of the nipple and areola in the 3rd type being possibly associated with drastic hormonal changes transpiring in puberty, pregnancy, and in men taking estrogen medication for prostatic adenocarcinoma. However, its etiopathogenesis is still undetermined and the role of hormones is not yet confirmed.[5] Generally, these lesions are asymptomatic; however, some may have mild pruritus.[6] Our patient has been taking oral contraceptive pills with no other associated dermatosis and can therefore be classified under the 3rd type. It may be prudent to request hormonal tests to investigate and establish whether hormones have indeed caused this dermatologic condition.

Despite its benign course, its cutaneous manifestation may pose significant alarm as it may mimic both benign and malignant lesions such as seborrheic keratosis, acanthosis nigricans, Paget's disease, superficial basal cell carcinoma, and Bowen's disease.[7] According to Balpande *et al*., NHNA is a diagnosis of exclusion.[1] The possibility of a malignant condition prompted a consult, and a histopathologic examination was warranted to establish diagnosis.

To date, there are < 50 published cases describing NHNA worldwide.[8] A total of 44 published cases on NHNA were reviewed and 64 patients were reported. Seventy-eight percent of these patients were female and were common in their second (29%) and third (42%) decades of life. In particular, 59% of the patients had bilateral breast affectation, most frequently involving both nipple and areola (42%). Only 13% presented with NHNA in their fourth decade of life, 39% had unilateral breast involvement, and 29% had areolar area involvement. These features were similar to our patient who was in her fourth decade with unilateral NHNA affecting her areola. Most patients had their lesions for more than 1 year (40%). Fourteen percent of the cases occurred after puberty, 9% during or after pregnancy, 1% appeared concomitantly with the use of oral contraception, whereas 68% were isolated cases or of unknown etiology. Lesions were predominantly asymptomatic, with only 10% complaining of mild-to-moderate pruritis, 1% of pain, and 1% with breastfeeding problems. Most of the literatures on NHNA were from Turkey, followed by India and Spain.

According to the Philippine Dermatological Society-Health Information System (PDS-HIS), there were no locally recorded cases of NHNA from 2011 to 2021 from all PDS-accredited institutions.[9] However, upon literature search, there was one published from the Philippines written by Soriano and Piansay-Soriano in 2014, on two patients with adolescent-onset NHNA. These cases were both seen by Dr. Piansay-Soriano, a PDS board-certified dermatologist at Davao Doctors Hospital, Section of Dermatology. Currently, Davao Doctors Hospital is not a PDS training institution; hence, cases from the said institution were not reflected in the PDS-HIS. Both patients were in their second decade of life when they presented with asymptomatic, diffuse, verrucous, hyperkeratotic, and hyperpigmented plaques affecting their bilateral areola with nipple sparing. These cases were associated with the onset of menarche. A combination of betamethasone dipropionate 0.05% and salicylic acid 3% ointment resulted in a 95% to 100% improvement in the lesions in both of the patients.[3] In contrast, our patient was a Filipino woman in her fourth decade of life with a mildly pruritic unilateral NHNA affecting only her right areola and was unaffected by her menstrual cycle and pregnancy.

NHNA is characterized histopathologically by hyperkeratosis, acanthosis, papillomatosis, sparse perivascular lymphocytic infiltrates, and keratotic plugging.[6] Our patient's histopathology result was consistent with NHNA as it presented most of its common features. Furthermore, there were clumps of melanin in the keratinocytes at the spinous layer of the epidermis in our patient that has not been previously reported in other published cases.

Currently, there are no specific guidelines for treating NHNA available.[1] Nevertheless, there are numerous topical and surgical therapeutic options for managing NHNA. Topical medications include keratolytic, calcipotriol, steroids, and retinoic acid.[3,5] Notably, patients treated with topicals have varied results and may require intermittent application as they are more prone to relapse.[3,6] In contrast, superior esthetic outcome and complete remission may be achieved through surgical

treatment which encompasses carbon dioxide laser, cryotherapy, surgical excision curettage, surgical removal with skin graft, and ablation with a radiofrequency surgical unit.[3,5] A review of 44 published cases showed that 52 patients received the following treatment in decreasing order of frequency: oral or topical retinoids (29%), glucocorticoids (23%), Vitamin $D_3$ analogs (23%), salicylic acid (10%), excision (10%), radiofrequency ablation (8%), cryotherapy (8%), hydroquinone (6%), urea (4%), carbon dioxide laser (4%), mammoplasty (2%), and oral minocycline (2%). Topical corticosteroids used were mometasone furoate 0.1%, betamethasone dipropionate 0.05%, and halobetasol propionate 0.05% applied twice daily with durations ranging from 4 to 40 weeks of application. Only 50% of patients treated with topical corticosteroids reported improvement of their lesions. Given the size of the lesion and the varied response to topical corticosteroids, including some treatment failures and relapses, we opted to treat our patient with twice daily application of Class 1 topical steroid, clobetasol propionate 0.05% ointment, for 2 weeks. This treatment was particularly chosen since the patient had previously applied betamethasone dipropionate plus mupirocin ointment intermittently with no improvement. To our knowledge, our patient was the first case to be treated with twice daily application of clobetasol propionate 0.05% ointment for 2 weeks which led to significant clinical improvement. This effect may be attributed to the antimitotic effect of topical corticosteroids. It is notable that the use of topical corticosteroids should be monitored and should not exceed 2–4 weeks to avoid local and systemic adverse effects.[10]

## Conclusion

We report a relatively uncommon presentation of NHNA in a Filipino woman in her fourth decade, with a mildly pruritic unilateral NHNA which involved only her right areola for 1 year. Although the prognosis is typically benign, it is advisable to conduct comprehensive history-taking, thorough physical examination, and skin biopsy to establish a diagnosis, particularly in instances where there is a persistent, progressively solitary pigmented lesion unresponsive to topical medications. The treatment options in various literatures encompass topical medication, laser therapy, and surgical interventions. However, in our case, we opted for clobetasol propionate ointment. While it is not a frequently reported treatment for NHNA, and despite the varied responses documented in most published cases concerning topical corticosteroids, our case yielded a significant clinical outcome.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

## References

1. Balpande G, Khatu S, Chavan D, Palaskar N. Bilateral nevoid hyperkeratosis of nipple: A report of two cases. Med J D Y Patil Vidyapeeth 2021;14:57.
2. Elloudi S, Lahlou A, Salim G, Baybay H, Rimani M, Mernissi FZ. Unilateral Nevoid Hyperkeratosis of the Nipple and Areola Treated Successfully With Carbon Dioxide Laser. Int J Clin Dermatol Res 2016; S1:001, 1-4.
3. Soriano LF, Piansay-Soriano ME. Naevoid hyperkeratosis of the nipple and areola: An extensive form in two adolescent Filipino females. Clin Exp Dermatol 2015;40:23-6.
4. Mehregan AH, Rahbari H. Hyperkeratosis of nipple and areola. Arch Dermatol 1977;113:1691-2.
5. Lamouaffaq A, Baybay H, Jouari OE, *et al*. Nevoid hyperkeratosis of the nipple mimicking a seborreic keratosis. J Dermat Cosmetol 2018;2:87-8.
6. Ning J, Zhang R, Zhu W. A case of unilateral nevoid hyperkeratosis of the nipple and areola. European Journal of Pediatric Dermatology 2021;31:47-9.
7. Dabas G, Guliani A, Vinay K, Radotra BD. Nevoid hyperkeratosis of male breast: Successful treatment with minocycline. Dermatol Ther 2019;32:e13019.
8. Mazzella C, Costa C, Fabbrocini G, Marangi GF, Russo D, Merolla F, *et al*. Nevoid hyperkeratosis of the nipple mimicking a pigmented basal cell carcinoma. JAAD Case Rep 2016;2:500-1.
9. Philippine Dermatological Society. Health Information Systems. Quezon City, Philippines: Philippine Dermatological Society; 2011. Available from: https://www.pdshis@outlook.com. [Last accessed on 2021 Jul 24, Last updated on 2021 Jul 13].
10. Gabros S, Nessel TA, Zito PM. Topical corticosteroids. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK532940/. [Last updated on 2023 Jul 10].