

BRIEF ARTICLE

A Case of Nevoid Hyperkeratosis of the Nipple in a Male Bahraini Patient

McKenzie A. Dirr MD¹, Sara Alkhanaizi MD², Fatema Khamdan MD¹

¹ Medical University of South Carolina, Charleston, South Carolina, USA

² Salmaniya Medical Complex, Department of Dermatology, Salmaniya district, Manama, Bahrain

ABSTRACT

Hyperkeratosis of the nipple/areola (HNA) is a wart-like thickening of the nipple and/or areola with concomitant hyperpigmentation. It can be further classified into groups based on etiology. Nevoid hyperkeratosis of the nipple/areola (NHNA) is a rare subtype with an unknown cause. It is a benign condition, which typically presents bilaterally in females often in times of hormonal changes. We present a case of a 51-year-old Bahraini male who presented with skin changes of the nipple and was ultimately found to have NHNA.

CASE REPORT

A 51-year-old Bahraini male presented to the dermatology clinic at Salmaniya Medical Complex with skin changes of the left nipple and areola for the past 11 months with pruritus and thickening of the skin. The changes were without pain, bleeding, discharge from the nipple, or constitutional symptoms. He did not have a history of tobacco or alcohol use, atopy, or breast cancer. Physical exam revealed hypopigmentation of the left nipple and areola with surrounding hyperpigmentation in the peripheral skin and areola (**Figure 1A**) with eczematous changes and lichenification and skin thickening. The right nipple and areola were without change (**Figure 1B**) and exam did not reveal tenderness, palpable masses, or axillary lymphadenopathy.

Tumor markers, including the common breast cancer tumor markers, cancer antigen 15-3 (CA 15-3) and carcinoembryonic antigen

(CEA), were negative, among other markers of neoplasm. Breast ultrasound and mammogram were unremarkable. A punch biopsy of the nipple showed epidermis and dermis without evidence of spongiosis, neutrophilic infiltrate, or atypical cells. Presence of scant surface bacterial colonies were noted. Given these findings, Paget's Disease and atopic dermatitis of the nipple were ruled out. A repeat histopathology section showed focal papillomatosis of the epidermis, irregular acanthosis and merged rete ridges, pseudocysts, and basketweave orthokeratotic hyperkeratosis (**Figures 2-3**). The findings combined with the clinical presentation confirmed the diagnosis of nevoid hyperkeratosis of the nipple and areola. Mometasone 0.1% ointment twice weekly and daily petroleum jelly under occlusion resulted in noticeable clinical improvement within 2 months. The patient was subsequently lost to follow up due to clinical improvement in his condition.



Figure 1A. Hypopigmentation with surrounding hyperpigmentation of the left nipple and areola.
Figure 1B. Normal pigment and architecture of the right nipple and areola.

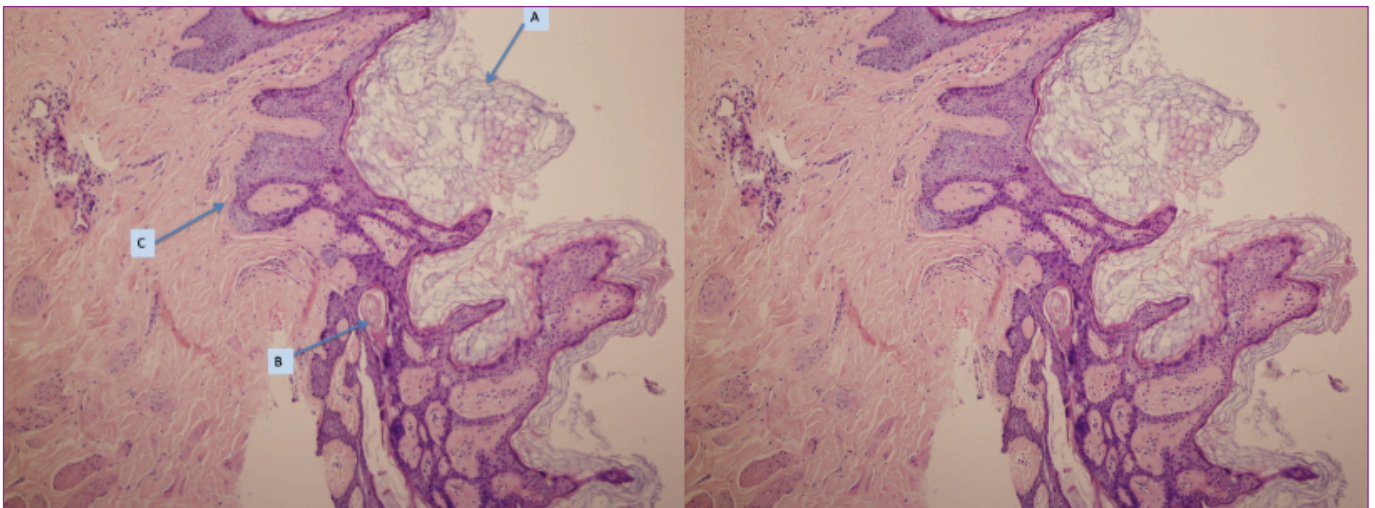


Figure 2A. Punch biopsy findings of the left nipple, showing (A) orthokeratotic hyperkeratosis, (B) pseudocysts, and (C) irregular acanthosis with fusion of rete ridges.

Figure 2B. Punch biopsy findings of the left nipple, with epidermis showing mild focal papillomatosis.

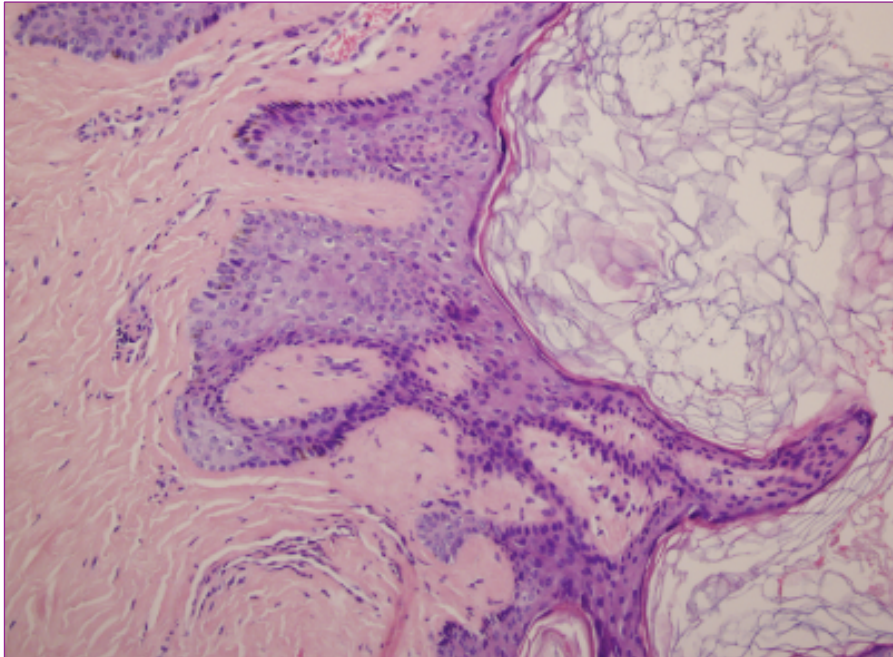


Figure 3. Punch biopsy findings of the left nipple without evidence of pagetoid cells.

DISCUSSION

Hyperkeratosis of the nipple/areola (HNA) is a rare, wart-like thickening of the nipple and/or areola with concomitant hyperpigmentation.^{1,2,3} In the system outlined by Levy-Frankel, the three subtypes include: Type I: expansion of an existing epidermal nevus into normal areola/nipple anatomy; Type II: dissemination of the underlying hyperkeratotic dermatosis, ichthyosis; and Type III: also known as nevoid, or idiopathic, the cause of which is unknown, often referred to as Nevoid Hyperkeratosis of the Nipple/Areola (NHNA).^{1,2,3,4} Alternatively, in the system outlined by Perez-Izquierdo, the two subtypes include: Type I, idiopathic, also known as NHNA, and Type II, which is a secondary manifestation of an underlying condition/etiology, including local, systemic, and drug-induced causes.^{2,3} To simplify the existing classifications, many experts suggest using a dichotomous scheme, with Type I describing an idiopathic primary condition, and Type II describing HNA as a

secondary manifestation of another condition, including hygienic practices, hormone therapy, pregnancy, atopic dermatitis, ichthyosis, nevi, etc.³ Specific reports of underlying HNA etiologies include other hyperkeratotic skin disorders, such as Darier's disease, acanthosis nigricans, chronic graft versus host disease, and T-cell lymphoma and medications such as oncologic therapies.^{1,2}

Nevoid HNA is a distinct condition which is not attributable to another dermatologic cause.⁴ Although NHNA is idiopathic, it is observed more frequently in times of hormonal changes, such as pregnancy, and has even been noted with hormonal therapies.^{1,2} Thus, hormonal changes are thought to play a role in the underlying etiology.^{2,4} NHNA most commonly affects females between 20 and 30 years of age, although males can also be affected.^{1,2} Exact incidence rate per country is not currently documented and estimates are unknown.³

Clinically, NHNA presents as an asymptomatic, irregular thickening and darkening of one or more nipple and/or areola without other skin disease.^{1,2,5} It has been described as a verrucous, or wart-like thickened area of skin, with a velvet-like or papillomatosis-like texture.³ It is most commonly bilateral, and the majority of cases present with involvement of the nipple/areola complex.^{2,3} It is a benign condition and does not impact life expectancy of affected individuals.^{1,3} Typically, no other complications are noted, aside from mild itching, presenting primarily as a cosmetic concern.^{1,3,4} However, it can cause obstruction of the anatomic structures, with resultant challenges in breastfeeding.

Diagnosis does not require lab evaluation.³ However, workup can rule out other etiologies or identify a primary cause such as cutaneous T-cell lymphoma.³ Dermoscopic features can include homogeneous brown pigmentation with scale and hyperkeratosis, red macules, pink patches, desquamating white areas, erosions, and commonly, papillomatosis.⁶ Furthermore, dermoscopic evaluation can rule out other diagnoses or help identify an underlying cause, such as Darier's Disease.³ It is imperative to rule out Paget's disease of the nipple, which is most commonly associated with an underlying malignancy of the breast arising from intraductal carcinoma.² The malignant cells spread to involve the nipple and/or areola and presents similarly to HNA, with a hyperkeratotic, scaling nipple with eczematous skin changes.² Important differentiating symptoms include the presence of nipple discharge, pain/discomfort, pruritus, or ulceration.^{2,3} As Paget's disease of the nipple can metastasize and become life threatening, it is important to rule out this condition with a mammogram, ultrasound, and biopsy in any patient presenting with similar signs and

symptoms.² Biopsy will show Paget's cells, large, clear cells with rounded nuclei and increased nuclear to cytoplasmic ratio.² Eczema, or atopic dermatitis of the nipple, is another cutaneous condition which can present similarly to HNA, which typically presents with pruritus and ill-defined borders without distortion of normal nipple anatomy.²

Histology of NHNA typically reveals epidermal orthokeratotic hyperkeratosis, plugging of keratin, elongated rete ridges with anastomoses, and filiform acanthosis in a downward projection, described as papillomatosis.^{1,2,3,4,6,7} Perivascular lymphocytic infiltrate, microabscesses, dermal melanophages and plasma cells, and spongiosis are also observed.³ Surface changes, including notable folding, can be observed microscopically.^{4,6}

If untreated, NHNA persists indefinitely.^{1,2,4} Various treatment options exist to improve the cosmetic appearance.^{1,2,3} While there is no gold-standard therapy, keratolytic topical treatments, such as lactic acid or salicylic acid, serve as first-line options.^{1,3} Other reports note improvement with topical retinoic acid, with a minimum trial of six months before efficacy can be evaluated, although recurrence was noted with discontinued treatment.^{1,2,3,8} One case report has noted effective response to topical steroids, but again, recurrence was noted.⁷ Furthermore, liquid nitrogen or carbon dioxide laser therapy has also proven efficacious in certain cases.^{1,2,3} Surgical procedures can be considered, such as curettage, surgical excision, and reconstruction with skin grafts, in select indicated cases such as recalcitrant disease in which breast surgery is appropriate.^{1,2,3} Counseling patients on disease course and managing expectations can lead to improved understanding and satisfaction.³

Conflict of Interest Disclosures: None

Funding: None

Corresponding Author:

McKenzie A. Dirr, MD
96 Jonathan Lucas Street, Suite 601, MSC 617,
Charleston, SC 29425
Phone: 843-792-2081
Email: mckenzie.dirr@gmail.com

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