

Unilateral nevoid hyperkeratosis of the nipple: A report of two cases

Veeranna Shastry, Jayadev Betkerur, P. A. Kushalappa

Department of Skin and STD, J. S. S. Hospital, Mysore, Karnataka, India.

Address for correspondence: Dr. Veeranna S, Department of Skin and STD, J. S. S. Hospital, Mysore, Karnataka, India.

E-mail: veerannashastry@yahoo.com.

ABSTRACT

Nevoid hyperkeratosis of the nipple and areola is an unusual condition. Two female patients aged 31 and 18 years presented with chronic unilateral warty lesions of the nipple. One patient had difficulty in breastfeeding from the affected side. A skin biopsy showed acanthosis, hyperkeratosis, papillomatosis, and lymphocytic infiltrate in the dermis. There was no significant improvement with topical tretinoin cream in both the patients.

Key Words: Nevoid hyperkeratosis of nipple and areola, Retinoids, Hyperkeratosis, Nipple

INTRODUCTION

Nevoid hyperkeratosis of nipple and areola (NHNA) is a rare condition, in which the skin of the nipple and/or areola becomes diffusely thickened, hyperpigmented, and covered with filiform or papular warty excrescences.^[1] We report two female patients with this rare condition.

CASE REPORTS

Case 1

A 31-year-old married woman noted a change in the appearance of the left nipple since 2 years, accompanied initially by mild itching. There was no history of discharge from the nipple. She had delivered a baby boy a year ago. Despite difficulty in breastfeeding from the affected side, she had continued to breast-feed the baby for nine months

after the delivery. She was not taking estrogen preparations. She had applied topical steroids and antifungal agents without any improvement.

On examination, the left nipple showed a warty surface and mild scaling [Figure 1]. There was minimal induration, and no tenderness. There was no discharge or lymphadenopathy. There were no changes in the areola. Breast examination was normal. The right nipple was normal. A skin biopsy taken from the left nipple showed hyperkeratosis, acanthosis, papillomatosis, and keratotic plugging [Figure 2]. She was treated with topical tretinoin 0.025% cream at night, and an emollient in the morning, without any significant change at the end of one month.

Case 2

An 18-year-old unmarried female presented with a growth on her left nipple, of one year's duration. There

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Figure 1: Case 1, warty change on the nipple



Figure 3: Case 2, warty plaque on the nipple

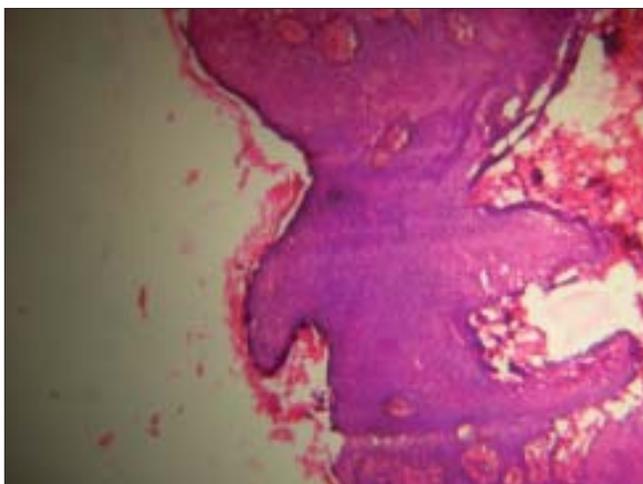


Figure 2: Histopathology showing acanthosis and papillomatosis (H & E 10x)

was a history of mild itching initially, but not of pain or discharge. She had received topical antibiotics and steroid creams with no improvement. There was no history of taking estrogen preparation. There was no personal history of atopy.

On examination, there was a brown warty, indurated plaque on the left nipple [Figure 3]. There was no tenderness, discharge, or lymphadenopathy. Breast examination was normal. The right nipple was normal. A skin biopsy was taken from the left nipple, and showed irregular acanthosis, papillomatosis, hyperkeratosis, and focal hypergranulosis. There was a dense lymphocytic infiltrate in the dermis. The patient was treated with topical 0.05% tretinoin cream, but there was no significant improvement after one month.

DISCUSSION

In 1938, Levy and Frankel described three distinct types of hyperkeratosis of the nipple and areola.^[1,2] Type I was hyperkeratosis as an extension of an epidermal nevus, type II was hyperkeratosis associated with other dermatoses (e.g., acanthosis nigricans, ichthyosis, lymphoma, chronic eczema, seborrhoeic keratosis or Darier's disease), while type III was nevoid hyperkeratosis, not associated with an epidermal nevus or other dermatoses.^[2] Perez-Izquierdo suggested an alternative classification of two types: idiopathic or nevoid, and secondary. The latter is due to local factors like acanthosis nigricans, verrucous nevus, seborrhoeic keratosis; ichthyosis, Darier's disease, chronic eczema or systemic factors like lymphomas, or drug related e.g., diethylstilbestrol and spironolactone.^[1] Mehanna *et al.* suggested that the term 'nevoid' should be replaced by 'idiopathic.'^[3]

Nevoid hyperkeratosis of the nipple or areola is a rare, idiopathic disorder with approximately 50 reported cases. Although it affects both men and women, approximately 80% of cases occur in women.^[4] It presents as hyperkeratotic, hyperpigmented plaques of the nipple and areola. It may also present as a verrucous lesion.^[4] There are several reports of unilateral nevoid hyperkeratosis,^[5] but the lesions are often bilateral. They may involve the nipple, areola, or both. Of the 45 cases of nevoid hyperkeratosis reviewed by Kubota *et al*, 17% involved the nipple, 25% the areola, and 58% both the nipple and the

areola.^[7] The lesions are generally asymptomatic, but occasionally they may be itchy.^[5] Difficulty in breast-feeding has been reported.^[6]

The etiology of NHNA is not known. A change in estrogen levels has been thought to precipitate this condition.^[8] The histopathological changes include orthokeratotic hyperkeratosis, papillomatosis, acanthosis, keratotic plugging, and mild perivascular lymphocytic infiltrate in the dermis.^[2] The differential diagnosis of NHNA includes epidermal nevus, acanthosis nigricans, chronic eczema, atopic eczema, seborrheic keratosis, Darrier's disease, Paget's disease, basal cell carcinoma, dermatophytosis, and Bowen's disease.^[2] There is no definite treatment for this condition. Various modalities such as topical corticosteroids,^[2] tretinoin, keratolytics,^[9] calcipotriol,^[10] etretinate,^[11] radiofrequency,^[12] surgery,^[13] and shave excision^[14] have been tried [Table 1].

We made the diagnosis of unilateral nevoid hyperkeratosis of nipple, based on clinical and histopathological features. Though the nipple shows minimal changes, the changes were significant when compared with the normal right nipple. Prolonged friction and rubbing of nipple can induce thickening and hyperkeratosis (jogger's or cyclist's nipple).^[1] This can mimic NHNA. However, our patients had minimal itching in the initial stage, and there was no history of chronic scratching or rubbing of the nipple. There had been no response to the application of a topical corticosteroid in the past. In both patients, histopathology showed benign epidermal hyperproliferative changes; there was no evidence of

pre-malignant or malignant changes. Treatment with topical tretinoin had no effect on the lesion.

We report these two patients of nevoid hyperkeratosis of the nipple and areola for the rarity of this condition. Although there is only one case of NHNA reported from India,^[15] the condition may be under-reported because of lack of awareness.

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Table 1: Treatment modalities of NHNA with outcome reported in literature

Authors	No. of patients	Treatment	Outcome
English JC <i>et al</i> ^[9]	1	Topical 12% lactic acid	Improved
Bayramgurur D <i>et al</i> ^[10]	2	Calcipotriol	Improved
Ortonne JP <i>et al</i> ^[11]	1	Etretinate	No improvement
Ozyazgani <i>et al</i> ^[12]	1	Radiofrequency	Improved
Milanovic <i>et al</i> ^[13]	1	Surgery	Improved
Swan MC <i>et al</i> ^[14]	1	Shave excision	Improved

*Nevoid hyperkeratosis of nipple and areola