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# Radical treatment of extensive nevoid hyperkeratosis of the areola and breast with surgical excision after mild response to topical agents: A case report



Ilaria Tocco-Tussardi (MD)<sup>a,b,\*</sup>, Nathalie Mobargha (MD, PhD)<sup>a</sup>, Franco Bassetto (MD)<sup>b</sup>, Vincenzo Vindigni (MD, PhD)<sup>b</sup>

<sup>a</sup> Department of Plastic and Maxillofacial Surgery, Uppsala University Hospital, 751 85 Uppsala, Sweden

<sup>b</sup> Clinic of Plastic and Reconstructive Surgery, Department of Neurosciences, University of Padova, Via Giustiniani 2, 35128 Padova, Italy

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## ABSTRACT

**INTRODUCTION:** Nevoid hyperkeratosis of the nipple and/or areola (NHNA) is a benign lesion with a female predominance and an aesthetically disturbing appearance. Spontaneous remission is not reported and medical treatments proposed so far have shown variable results.

**PRESENTATION OF CASE:** We describe a rare case of an extensive variant of NHNA covering almost the entire breasts' surface. At present, only three other reports are present in the literature. Medical treatment proved not completely effective and the patient was also affected by a significant breast asymmetry-hypertrophy. Therefore, NHNA was managed surgically with excision of the areolar affected portions while performing breast reduction-lift. The result was satisfactory and without recurrence of lesions at 5-year follow-up.

**DISCUSSION:** This case reported favorable outcomes of surgery for NHNA. Reports of success with these procedures are still limited, but the promising results in terms of radicality and aesthetic outcome suggest it should be offered to patients as a viable therapeutic option.

**CONCLUSION:** Indications for surgical treatment of NHNA can be: unsatisfying response to topical agents; young patients who want to restore the aesthetic appearance of the breast; and patients with concomitant indication for corrective surgery of the breast. Advantages are: predictable time of healing; predictable final result; radical excision of the affected tissue; and possibility of histologic analysis of the whole areola. In rare cases of lesions extending to the breast, preliminary treatment with topical agents can limit the extent of excision. Management and treatment should always be tailor-made for each individual case.

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## 1. Introduction

Nevoid hyperkeratosis of the nipple and/or areola (NHNA) is a rare lesion of unknown etiology, most predominant in the female gender between puberty and the third decade [1,2]. Although benign, its clinical appearance (dark brown plaques and hyperkeratotic skin) can be extremely disturbing, especially if extending beyond the nipple/areolar area. In these cases, surgical approach can be considered as a valid therapeutic option, alone or in combination with topical treatment, to restore the aesthetic appearance especially in the young. We describe a rare case of bilateral NHNA with an extensive involvement of the areolas and breasts in a pregnant female with significant breast asymmetry.

## 2. Presentation of case

A 33-year-old female was referred to the Clinic of Plastic Surgery for evaluation of hyperpigmented, diffuse papillomatous plaques over the areola and breast bilaterally that had been present for 2 months (Fig. 1). She was in the second trimester of her first pregnancy. The patient described the lesions as starting as a thickening of both areolas and then progressing to involve much of the breasts, and associated with mild pruritus. She was otherwise healthy except for a moderate fibrocystic breast condition, had no known allergies, and was receiving no drug therapy. There was no evidence of associated endocrinopathy, dermatosis, or lymphomas, and no family history of similar lesion.

On physical examination, hyperkeratotic, verrucous, and brownish-pigmented plaques were found involving both areolas and breasts especially on the right side, but not adherent to the underlying structures. There was no significant lymphadenopathy. Their nipples were normal and with no discharge. She presented

\* Corresponding author at: Department of Plastic and Maxillofacial Surgery, Uppsala University Hospital, 75185 Uppsala, Sweden.

E-mail address: [iilaria.tocotussardi@gmail.com](mailto:iilaria.tocotussardi@gmail.com) (I. Tocco-Tussardi).



**Fig. 1.** Bilateral nevoid hyperkeratosis of the areola and breast in a 33-year old female.



**Fig. 2.** Five-year follow-up after combination of topical agents and surgical treatment (removal of affected areolar areas concomitant with right reduction mammoplasty and left mastopexy).

breast hypertrophy and a remarkable size asymmetry, associated with a third-degree ptosis (according to Regnault) on the right breast and a second-degree ptosis on the left.

Punch biopsy specimens were obtained from both breasts, superior to the areola. Histopathologic examination revealed hyperkeratosis, papillomatosis, dermal fibrosis, and occasional melanophages, with a final diagnosis of nevoid hyperkeratosis. In agreement with the patient the treatment was deferred until delivery.

Following delivery (she never lactated), the patient underwent a 3 month-course of 2% hydroquinone topical treatment, followed by a 3-month course of 4% kojic acid. The pigmentation on the breast decreased within 8 weeks and improved significantly in 20 weeks. However, the hyperkeratotic plaques involving the areolas persisted almost unvaried. As the patient had already expressed the will to undergo surgery to correct breast ptosis and asymmetry, a concomitant surgical excision of the affected areolar tissue was discussed and agreed. Hence, 11 months after delivery the patient underwent surgical treatment. We performed a right reduction mammoplasty according to McKissock excising the areolar affected portions and 435 gr of mammary gland. Left inverted “T” breast lift (mastopexy) and removal of the areolar affected portions allowed for the achievement of a symmetric result. Both areolas were reduced to the diameter of 5 cm. Definitive histologic finding confirmed nevoid hyperkeratosis. The patient was hospitalized for 5 days and she was healed by postop day 18 with no complications. No recurrence has been observed during the 5-year follow-up (Fig. 2), over which the patient had no other pregnancies.

**3. Discussion**

Nevoid hyperkeratosis has been described as a variant of hyperkeratosis of the nipple/areola and is characterized by: brown plaques over the nipple (17%), areola (25%), or both (58%); association with hyperkeratotic thickening of the skin; occurrence in females in the second and third decades of life usually in connection with sharp hormonal changes (menarche/pregnancy); a bilateral (80%) or unilateral (20%) fashion; and no apparent etiology [1,2]. Nevoid hyperkeratosis is always a diagnosis of exclusion (Table 1) and histologic detection of specific features (hyperkeratosis, acanthosis, and papillomatosis with occasional keratotic plugging) come as confirmation [1–3]. Differential diagnosis of lesions occurring during pregnancy should consider physiologic and para-physiologic changes of the nipple and areola, such as enlargement, hyperpigmentation, secondary areolae, and the

**Table 1**

Differential diagnosis for nevoid hyperkeratosis of the nipple and/or areola.

- a) Common dermatologic disorder; (epidermal nevus, seborrheic keratosis, nevus sebaceous, allergic dermatitis, mycosis fungoides);
- b) Hyperkeratosis secondary to:
  - Local disease (acanthosis nigricans);
  - Systemic disorder (ichthyosis, Darier's disease);
- c) Diseases of the nipple-areola complex (Paget's disease, Mondor's disease);
- d) Others
  - Underlying malignancy;
  - Endocrinopathy;
  - Drug-related reactions (e.g. to spironolactone or diethylstilbestrol therapy).

recently described pregnancy-associated hyperkeratosis of the nipple [4].

The present patient represented a peculiar clinical challenge as only three similar cases have been described in the literature. Nevoid hyperkeratosis affecting the areolas and peri-areolar skin can be considered an extensive variant of NHNA. All cases so far occurred in adolescent girls with onset soon after menarche while our case is the first report of extensive nevoid hyperkeratosis with onset during pregnancy. Of the three cases, two were managed with a combination ointment of 0.05% betamethasone and 3% salicylic acid [5]. The authors report the treatment achieved almost complete remission, however lesions recurred after cessation, even if in a minor extension. The third case lacks of information on the final outcome, but the authors report that a treatment with topical steroids had proved unsuccessful [6].

Conservative treatment has traditionally been the primary therapeutic approach to NHNA and a number of different agents and modalities has been reported through years (Table 2)[4–15]. Success rates, however, have varied greatly: early results have been usually acceptable (except for tretinate) [16], but the final esthetic outcome was often not so satisfactory, and longer follow-up were either not available or showed recurrences after cessation [5,8,10]. Therefore, there is no uniformly accepted topical treatment among the many proposed. In our case, we used a combination of topical hydroquinone with kojic acid which induced a good response on hyperpigmentation of the breast, but was ineffective on hyperkeratosis of the areola.

**Table 2**  
Operative overview on therapeutic options for nevoid hyperkeratosis of the nipple and/or areola.

Condition	Conservative treatment	Semi-conservative treatment	Surgical treatment
NH of the nipple	Ammonium lactate Low-potency steroids Tretinoin	CO <sub>2</sub> laser Cryotherapy Radiofrequency	Curettage
NH of the areola	Calcipotriol Isotretinoin Lactic acid Retinoic acid Salicylic acid Urea	ablation	Excision Reconstruction with skin graft Shaving
Extensive NH (areola and breast)	<i>For hyperpigmentation:</i> Hydroquinone Kojic acid Low-potency steroids Salicylic acid	Not reported	

Although NHNA is a condition known since 1923, it was not until 2005 that surgical treatment started to be experimented after being advocated, and only two other reports on surgical treatment of NHNA are present in the literature. One patient was affected by bilateral nevoid hyperkeratosis of the areolas and, after being unsuccessfully treated with keratinolytics, underwent excision of the hyperkeratosis and reconstruction of both areolas with full-thickness skin grafts from the inguinal regions [17]. She was reported as fully healed at postop day 10 and free from recurrence at 12-month follow-up. The other patient received a primary surgical management of a bilateral nevoid hyperkeratosis of the nipples and areolas with surgical shaving of the nipple and areola on one side, and surgical resection of the areola followed by reconstruction with full-thickness skin graft on the other side [18]. At 24-month follow-up there was no evidence of recurrence and the result is aesthetically valid.

This case reported favorable outcomes of surgery for nevoid hyperkeratosis. Excision of the areolar affected portions achieved a complete eradication of the disease with an acceptable aesthetic result. Therefore, we can state that all cases so far confirm surgical treatment as a radical, fast solution with a good esthetic result and long-term outcome. Compared to shave treatment, excising is superior because of more predictable time of healing, more predictable final esthetic result, radical excision of the affected areola without residue, and possibility of getting the whole areola for definitive histologic analysis [19]. The specific intervention should be tailored to the individual patient, her general conditions, extensions of the disease, and possible contraindications to surgical treatment. In cases of isolated areolar involvement, excision could be offered as first-line treatment.

Table 2 summarizes the panel of therapeutic options available for nevoid hyperkeratosis.

#### 4. Conclusion

In clinical practice, patients affected by NHNA can be counselled on surgical treatment (removal of the areola ± reconstruction with a skin graft) as a reasonable option. Surgical treatment is especially indicated in case of: unsatisfying response to topical agents; young patients who want to restore the aesthetic appearance of the breast; and patients with a concomitant indication for functional/cosmetic surgery. In rare cases of NHNA extending to the breast, preliminary treatment with topical agents can prove effective to clear hyperpigmentation and limit excision to the areolar area. Management and treatment should always be tailor-made for each individual case according to the different therapeutic options.

#### Conflict of interest statement

None to disclose.

#### Ethical Approval

The present study is not a research study.

#### Author contribution

Dr. Tocco-Tussardi contributed to the present work by designing the Report, acquiring, analyzing, and interpreting the clinical data, drafting the article, and finally approving the version to be submitted;

Dr. Mobargha contributed to the conception and design of the Report, revised critically the article content, and gave final approval of the version to be submitted;

Dr. Basssetto contributed to the conception and design of the Report, revised critically the article content, and gave final approval of the version to be submitted;

Dr. Vindigni contributed to the Report by acquiring and interpreting the clinical data, revised critically the article content, and gave final approval of the version to be submitted.

#### Care guidelines statement

The authors declare this case report is compliant with the CARE Guidelines, available at: <http://www.care-statement.org/>.

#### References

- [1] R.S. Krishnan, T.A. Angel, T.R. Roark, S. Hsu, Nevoid hyperkeratosis of the nipple and/or areola: a report of two cases and a review of the literature, *Int. J. Dermatol.* 41 (2002) 775–777.
- [2] A.H. Mehregan, H. Rahbari, Hyperkeratosis of nipple and areola, *Arch. Dermatol.* 113 (1977) 1691–1692.
- [3] H. Obayashi, T. Tsuchida, S. Ikeda, Hyperkeratosis of the nipple and areola, *Rinsho Dermatol.* 40 (1998) 147–150.
- [4] H.W. Higgins, J. Jenkins, T.D. Horn, G. Kroumpouzos, Pregnancy-associated hyperkeratosis of the nipple: a report of 25 cases, *JAMA Dermatol.* 149 (2013) 722–726.
- [5] L.F. Soriano, M.E. Piansay-Soriano, Naevoid hyperkeratosis of the nipple and areola: an extensive form in two adolescent Filipino females, *Clin. Exp. Dermatol.* 40 (2015) 23–26.
- [6] F. Succaria, M. Rosenbaum, L. Goldberg, M. Mahalingam, Dark brown plaques and patches on the breast and areola in a 14-year-old female. Nevoid hyperkeratosis of the areola and breast, *Am. J. Dermatopathol.* 37 (2015) 621–622.
- [7] D. Bayramgurler, N. Bilen, R. Apaydin, C. Ercin, Nevoid hyperkeratosis of the nipple and areola: treatment of two patients with topical calcipotriol, *J. Am. Acad. Dermatopathol.* 46 (2002) 131–133.

- [8] P. Toros, M. Onder, M. Gurer, Bilateral nipple hyperkeratosis treated successfully with topical isotretinoin, *Aust. J. Dermatol.* 40 (1999) 220–222.
- [9] J.C. English 3rd, N.V. Coots, A man with nevoid hyperkeratosis of the areola, *Cutis* 57 (1996) 354–356.
- [10] J.M. Pérez-Izquierdo, J.J. Vilata, J.L. Sánchez, E. Gargallo, F. Millan, A. Aliaga, Retinoic acid treatment of nipple hyperkeratosis, *Arch. Dermatol.* 126 (1990) 687–688.
- [11] P. Mayock, Hyperkeratosis of the nipple, *Arch. Dermatol.* 114 (1978) 1245.
- [12] D.S. Kuhlman, S.J. Hodge, L.G. Owen, Hyperkeratosis of the nipple and areola, *J. Am. Acad. Dermatol.* 13 (1985) 596–598.
- [13] J. Mitxelena, J.A. Raton, I. Bilbao, J.L. Diaz-Perez, Nevoid hyperkeratosis of the areola in men: response to cryotherapy, *Dermatology* 199 (1999) 73–74.
- [14] A. Busse, M. Peschen, E. Schöpf, W. Vanscheidt, Treatment of hyperkeratosis areolae mammae naeviformis with the carbon dioxide laser, *J. Am. Acad. Dermatol.* 41 (1999) 274–276.
- [15] I. Ozyazgan, O. Kontas, A. Ferahbas, Treatment of nevoid hyperkeratosis of the nipple and areola using a radiofrequency surgical unit, *Dermatol. Surg.* 31 (2005) 703–705.
- [16] J. Ortonne, P. El Baze, L. Juhlin, Nevoid hyperkeratosis of the nipple and areola mammae: ineffectiveness of tretinoin therapy, *Acta Derm. Venereol.* 66 (1986) 175–177.
- [17] R. Milanovic, K. Martic, S. Stanec, R. Zic, Z. Vlajcic, Z. Stanec, Surgical treatment of nevoid hyperkeratosis of the areola by removal of the areola and reconstruction with a skin graft, *Ann. Plast. Surg.* 54 (2005) 667–669.
- [18] A. Foustanos, K. Panagiotopoulos, D. Ahmad, K. Konstantopoulos, Surgical approach for nevoid hyperkeratosis of the areola, *J. Cutan. Aesthet. Surg.* 5 (2012) 40–42.
- [19] M.C. Swan, S.E. Gwilym, K. Hollowood, V. Venning, O. Cassell, Treatment of nevoid hyperkeratosis of the nipple and areola by shave excision, *Ann. Plast. Surg.* 53 (2004) 510–512.

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