

Case Report

Resolved Peristomal Erosive Papulonodular Dermatitis Mimicking Nevoid Hyperkeratosis of the Nipple and Areola

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Abstract

Introduction

Nevoid hyperkeratosis of the nipple and areola (NHKNA) is a rare cutaneous entity with a distinct clinical and histological presentation. The type II form of this condition can result from various dermatoses, such as irritant contact dermatitis. Erosive papulonodular dermatitis is a chronic irritant dermatitis that often occurs in areas of occlusion and maceration, such as peristomal skin. Pseudoverrucous papules and nodules are a variant of erosive papulonodular dermatitis and have a non-specific histologic pattern of reactive hyperplasia.

Case Presentation

We present a case of a patient with resolved peristomal erosive papulonodular dermatitis who presented status-post ileostomy reversal with clinical and histologic findings classically seen in NHKNA.

Conclusion

In type II NHKNA, treatment of the primary dermatosis typically leads to resolutions. In the case of our patient, removal of the offending agent via colostomy reversal and barrier protection led to the resolution of the lesions.

Keywords

keratosis; dermatitis; nevoid hyperkeratosis of the nipple and areola; NHKNA; erosive papulonodular dermatitis; peristomal dermatoses; pseudoverrucous papules and plaques

Introduction

Nevoid hyperkeratosis of the nipple and areola (NHKNA) is a rare condition, with fewer than 50 reported cases since it was first described in 1938.¹ The hyperkeratotic, darkly-pigmented verrucous papules involving the nipple-areola complex can be idiopathic or arise as an extension of an existing nevus or other skin condition. Various skin dermatoses have been described in association with NHKNA, including chronic irritant contact dermatitis.

Erosive papulonodular dermatitis is a form of irritant contact dermatitis seen in areas of chronic moisture in the presence of an irritant,

such as urine or feces. This form has also been referred to as ileostomy-associated chronic papillomatous dermatitis (CPD).² It frequently occurs on occluded skin, as these areas are more prone to maceration. Rare forms like pseudoverrucous perianal papules and plaques and granuloma gluteale infantum occur on the buttocks or groin, as their names would suggest. However, any skin subjected to this milieu is susceptible to such changes. One such setting is perilesional skin surrounding urostomies, ileostomies, and colostomies.³

The histologic appearance of erosive papulonodular dermatitis is often that of non-specific

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Figure 1. The initial presentation shows a confluent peristomal plaque of red-brown verrucous papules.

reactive hyperplasia. This appearance includes psoriasiform or pseudoepitheliomatous hyperplasia and mixed superficial perivascular infiltrate.⁴ In contrast, NHKNA has a relatively specific histologic pattern. The epidermal rete are markedly elongated with variable papillomatosis. The basal layer of the epidermis is hyperpigmented without associated melanocytic proliferation. Here we present a case of a patient with a history of erosive papulonodular dermatitis of peri-ileostomal skin. Following the reversal of his ileostomy, these lesions developed classic clinical and histologic features of NHKNA.

Case Presentation

A 52-year-old man presented to the hospital for evaluation of an eruption surrounding his abdominal ileostomy. The patient initially had a colostomy placed secondary to colonic obstruction due to diverticulitis. This placement was converted into an ileostomy 4 months later,

with subsequent reversal 8 months later. The initial colostomy site had healed well, but an eruption had developed at the site of his ileostomy prior to take down. The patient reported his ileostomy bag had fit poorly, and his skin had constantly been in contact with stomal effluent. The initial eruption had been painful and bled, though these symptoms had resolved post-reversal.

Physical examination of the abdomen was notable for a confluent peristomal plaque of red-brown verrucous papules. The location of the ileostomy itself was otherwise healing well (**Figure 1**). Erosive papulonodular dermatitis secondary to chronic maceration was initially suspected. As the ileostomy had already been reversed, frequent application of petrolatum jelly was recommended. Minimal improvement was observed at the patient's 1-month follow-up when a shave biopsy was obtained (**Figure 2**). A histologic examination demonstrated

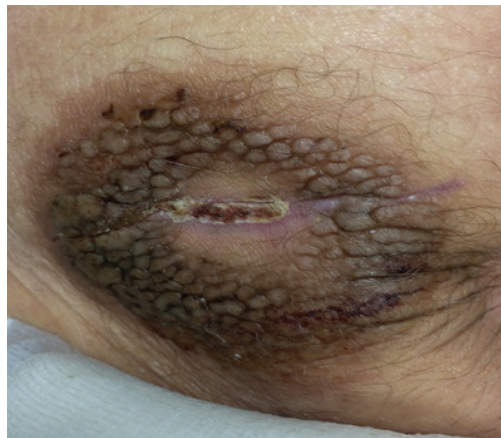


Figure 2. The lesion at the 1-month follow-up shows persisting verrucous brown papules.

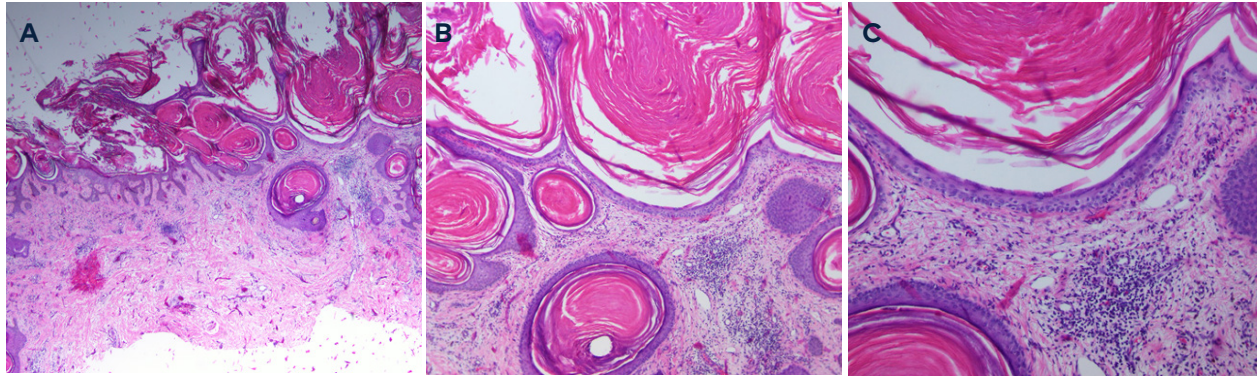


Figure 3. A. The biopsy H&E (4x) shows papillomatosis, rete elongation, and hyperpigmentation of the basal layer. **B.** The biopsy H&E (10x) shows orthokeratotic hyperkeratosis and keratotic plugging. **C.** The biopsy H&E (40x) shows sparse perivascular mixed inflammatory infiltrate.

epidermal acanthosis, papillomatosis, and hyperkeratosis on hematoxylin and eosin stain (H&E). Hyperpigmentation of the basal layer was observed (**Figures 3A-C**). The Periodic Acid Schiff (PAS) was negative for fungal or hyphal elements (**Figure 4**). This constellation of histopathologic findings in the context of the clinical appearance of the lesions was consistent with NHKNA-like change.

Discussion

Chronic irritant contact dermatitis resulting from contact with feces, urine, or both can manifest in various clinical morphologies. More rare forms include Jacquet's dermatitis, granuloma gluteal infantum, and pseudoverrucous papules.⁵ The distribution of these entities is typically the buttocks, perianal skin, and/or perineum, as these areas are in direct apposition to the offending agents.³ Multiple shiny, smooth, red, moist, round papules and nodules with erosions are clinically typical, often described as "pseudoverrucous." These

pseudoverrucous lesions may appear as shiny, moist, white-gray verrucous papules, nodules, and plaques. Chronic lymphedema, such as elephantiasis nostra verrucosa, can present similarly with hyperkeratosis, papillomatosis, and verrucous hyperplasia.⁴⁻⁶

The pathophysiology underlying chronic irritant contact dermatitis is due to a persistent moist environment resulting in skin maceration. The skin is further aggravated by occlusion, for example, by diapers or surgical dressings. This combination of moisture and occlusion enhances the skin's susceptibility to urine and feces irritants. Proteases and lipases in fecal material are the primary culprits, which become activated as pH increases. Ammonia in urine further increases local pH, heightening irritation. Patients with Hirschsprung's disease status-post ileoanal anastomoses presented with perianal pseudoverrucous papules in one case series. All of the patients had persistent diarrhea following surgery. Diarrhea has a higher concentration of active enzymes in patients with shorter

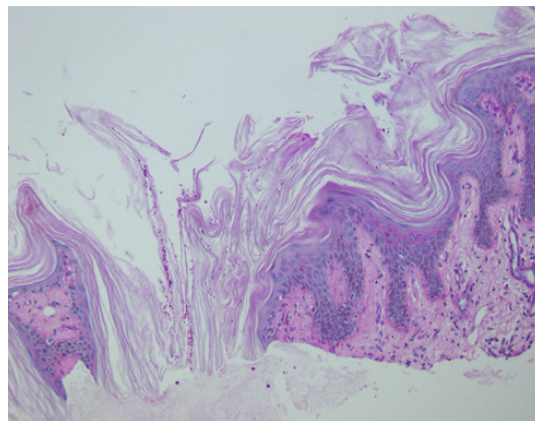


Figure 4. The biopsy PAS (4x) was negative for pathogenic fungal elements. Fibrosis along with dilated vascular and lymphatic spaces can be observed.

bowels, as decreased absorption time results in a more alkaline pH.³ Localized lymphedema from scarring may play a role in the pathogenesis and lead to depressed cell-mediated immunity.^{2,6} Elephantiasis nostra verrucosa has similar clinicopathological findings supporting a possible role of lymphatic stasis.^{2,6}

The histological pattern in these conditions is non-specific and may have variable degrees of acanthosis, papillomatosis, spongiosis, surface erosions, papillary edema, ectatic vascular, lymphatic channels, and mixed perivascular inflammatory infiltrate. Fungal and bacterial cultures are typically negative. However, regional contamination by urine or feces may be isolated. When pseudoverrucous papules are present, psoriasiform hyperplasia, acanthosis, parakeratosis, and hypogranulosis, in combination with a mixed superficial perivascular infiltrate consistent with reactive hyperplasia, can be observed.^{3,4} Human papillomavirus (HPV) has been detected in chronic papillomatous dermatitis, while HPV-infected keratinocytes will often show upregulation of p16 immunohistochemistry.² No HPV testing or p16 immunohistochemistry was performed on our patient's biopsy.²

Classically considered a form of diaper dermatitis, the clinicopathologic changes have also been reported in areas of chronic moisture and irritation, such as chronically draining wounds, chronic application of benzocaine, and as a consequence of urostomy or colostomy leakage.⁷ Distal procedures such as sigmoid colectomies retain the water-absorbing and storage function of the colon and so expel a relatively solid stool. Conversely, proximal colostomies and ileostomies have more frequent and runny outflows rich in proteolytic enzymes from the pancreas and biliary tract. Without barrier protection, erosions and maceration quickly develop, compromising pouch adhesion, worsening leakage, and further exacerbating the problem.⁸ In 1988, Erik Borglund et al classified peristomal skin findings at urostomy sites. The proposed classification system included 2 broad categories: erythematous-erosive and pseudoverrucous changes. Of the two-thirds of patients with skin changes, the majority had either erythematous-erosive disease alone or in combination with pseudoverrucous changes.⁹ Histologically, most of the reported cases of

stomal dermatosis show features of chronic irritant contact dermatitis or, in long-standing cases, a more non-specific pattern of lichen simplex chronicus. Pseudoverrucous papules and nodules appear as acanthomatous dermatitis with papillomatosis or pseudoepitheliomatous hyperplasia.¹⁰

NHKNA was initially described by Tauber et al in 1923.¹¹ In 1938, Levy-Frankel subdivided the condition into 3 clinical subtypes. In type I, changes result from the extension of an existing epidermal neoplasm into the nipple-areola complex. These would include epidermal nevi, organoid nevi, and seborrheic keratoses.¹² Hyperkeratosis of the nipple and areola that occurs coincidentally with other skin diseases (type II) is typically seen related to cornification disorders like ichthyosis, acanthosis nigricans, and Darier's disease. Cases related to chronic dermatoses, eczema, hormonal changes, internal malignancy, and cutaneous T-cell lymphoma have also been reported.¹³ In addition, diethylstilbestrol and spironolactone are medications that have been implicated in cases of type II hyperkeratosis of the nipple and areola.¹⁴ As in type I, skin involvement is typically beyond that of the nipple-areola complex alone. Unlike type I or II, type III is often bilateral and typically appears in the second or third decade following menarche or during pregnancy, or in men with prostate cancer treated with diethylstilbestrol.¹⁵ None of the type III cases reviewed demonstrated involvement beyond the nipple and areola complex.¹³

Hyperkeratosis of the nipple and areola typically presents as hyperkeratotic, hyperpigmented plaques of the nipple and/or areola. The plaques are often darkly pigmented and verrucous. Yellowish discoloration or desquamation of the areas may also be seen. The lesions may also appear verrucous and can involve one or both areolae and/or nipples.¹³ Our patient had confluent brown verrucous papules and plaques on the peristomal abdomen that looked clinically very similar to NHKNA.

Characteristic histologic findings include orthokeratotic hyperkeratosis with occasional keratotic plugging. Rete ridges are elongated and anastomose with prominent and variable filiform papillomatosis. The basal layer is hyperpigmented without melanocytic pro-

liferation. Mild perivascular lymphocytic infiltrate may be seen in conjunction with these classic findings.^{1,12} Type I and II hyperkeratosis of the nipple and areola can exhibit specific histopathological features of the primary skin disease or neoplasm and usually involve skin beyond that of the nipple-areola complex. This diagnosis shares histopathological features with both epidermal nevi and acanthosis nigricans. Thus, it is distinguished by its location and clinical presentation. Given the history of a poorly fitting ileostomy bag with leaking stromal contents and subsequent eruption and ileostomy reversal showing clinicopathologic findings consistent with NHKNA, we arrived at our diagnosis.

Case reports and series have indicated an association of NHKNA with mycosis fungoides. These were cases in which patients with an existing diagnosis of mycosis fungoides manifested with clinical changes consistent with NHKNA. Histologic evaluation in these cases has shown greater variability. Some had classic NHKNA-like changes while others had histopathologic features of mycosis fungoides (CD3+ intraepidermal lymphocytes, CD4 predominance, and loss of CD7 positivity). There have been several reports of hyperkeratotic lesions of the nipple and areola indicating unilateral or early lesion MF. However, these cases all had classic histologic features of mycosis fungoides.¹²

Due to the rarity of this diagnosis, treatment of this condition is anecdotal. In the case of type II NHKNA, treatment of the primary dermatosis typically leads to resolutions. NHKNA treatment options include keratolytics, retinoids, cryosurgery, and excision. Plastic surgeons have performed excisions, but no data on the outcomes exist.¹⁵ Topical steroids yield variable results. Fortunately, the condition is typically asymptomatic and requires no treatment.¹ In the case of our patient, removal of the offending agent via colostomy reversal and barrier protection led to resolution of the lesions.

Conclusion

We present this case as an unusual presentation of peristomal pseudoverrucous papules and nodules mimicking NHKNA both clinically and histologically.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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