Porokeratoma

Sarah N. Walsh, MD, Mark A. Hurt, MD,† and Daniel J. Santa Cruz, MD†*

Abstract: Cornoid lamellation is a specific disorder of epidermal maturation manifested by a vertical "column" of parakeratosis and is the hallmark of porokeratosis. The cornoid lamella is characterized by a ridgelike parakeratosis. We present 11 patients with solitary lesions of a distinct pattern of cornoid lamellation. The mean age at presentation clinically was 57 years; there were 9 men and 2 women. The duration of the lesions ranged from 3 months to 5 years (mean of 23 mo). All lesions were solitary, distributed mainly on the distal upper and lower limbs, and were clinically described as hyperkeratotic plaques or nodules; some were verrucous. Histologic examination showed a well-defined lesion characterized by acanthosis and verrucous hyperplasia with prominent multiple and confluent cornoid lamellae. No additional lesions were identified in any patient, with a mean follow-up duration of 34 months. No personal or family history of porokeratosis was elicited and no immunosuppressive conditions were noted. These lesions with multiple and confluent cornoid lamellae represent benign acanthomas with features of porokeratosis. As a solitary tumorlike lesion, it is akin to warty dyskeratoma and epidermolytic acanthoma, thus we have coined the term *porokeratoma*.

Key Words: porokeratosis, cornoid lamella, warty dyskeratoma, epidermolytic acanthoma, acanthoma, case series

(*Am J Surg Pathol* 2007;31:1897–1901)

Epidermolytic hyperkeratosis and acantholytic dyskeratosis were once thought to be the defining histologic features of generalized disease processes, as with bullous congenital ichthyosiform erythroderma and Darier and Grover disease. Subsequently, it was noted that these findings were identified in conditions with multiple lesions that were both localized and systematized.[1,2] With the recognition of epidermolytic acanthoma and warty dyskeratoma, it is now widely accepted that these microscopic patterns occur as solitary lesions with tumorlike clinical presentations and distinct clinicopathologic conditions.[17,18]

Cornoid lamellae are the manifestations of a localized clonal abnormality in epidermal maturation. They are seen classically in porokeratosis, a genetically predisposed disorder of cornification. There are several well recognized variants, including porokeratosis of Mibelli (PM), porokeratosis palmaris et plantaris disseminata (PPPD), linear porokeratosis (LP), punctate porokeratosis (PP), and disseminated superficial (actinic) porokeratosis (DSAP).[12,9,13,14,16]

Each of these variants has distinctive clinical and histologic features but all are unified by the presence of cornoid lamellae. We present 11 cases of a solitary tumorlike lesion with a distinct pattern of cornoid lamellation found in patients without a history of porokeratosis or immunosuppression.

MATERIALS AND METHODS

The cases were collected prospectively from our daily dermatopathology practice between July 2001 and March 2007. Hematoxylin and eosin-stained sections were examined and deeper levels were cut on all cases.

Patient demographics, lesion characteristics, and differential diagnoses were gathered from the submitted specimens. The treating physicians were contacted for further clinical information, including lesion duration, prior diagnosis of porokeratosis, history of immunosuppressive conditions or drugs, treatment, and follow-up (Table 1).

RESULTS

The patients ranged in age from 31 to 77 years, with a mean age of 57.2 years. Of the 11 cases, there were 9 men and 2 women.

The lesions were distributed as follows: upper extremities [forearm (1), hand (1), thumb (1)], lower extremities [posterior leg (1), calf (1), anterior thigh (1)], and one each on the forehead, lower lip, chest, buttocks, and intergluteal cleft. The known duration of lesions ranged from 3 months to 5 years, with a mean of 23 months. In 8 cases, the lesion duration was not available. Follow-up information ranged from 1 month to 67 months, with a mean time of 34 months.

On the basis of clinical information provided, the lesions were described as solitary scaling hyperkeratotic plaques, papules, or nodules, some appearing verrucous.

Several clinical diagnoses were offered. In order of frequency, these included squamous cell carcinoma (4),

From the *Department of Pathology and Immunology, Barnes-Jewish Hospital/Washington University School of Medicine; and †Cutaneous Pathology, WPC Laboratories, Inc, St Louis, MO.
Funding Sources: None.
The authors have no conflict of interest to disclose.
The abstract to this paper has been presented as a poster at the 2006 American Society of Dermatopathology Annual Meeting in Chicago, IL from October 26 to 29, 2006.
Reprints: Daniel J. Santa Cruz, MD, 2326 Millpark Dr St Louis, MO 63043 (e-mail: dsantacruz@aol.com)

TABLE 1. Clinical Findings in Patients With Porokeratoma

Case	Age	Sex	Location	Duration	Clinical Differential Diagnosis	Single/ Multiple	Persistent Lesions (f/u, mo)
1	77	M	Right IGC	Not stated	VV	Single	No (67)
2	77	F	Left posterior leg	6 mo	AK, SCC	Single	No (66)
3	61	M	Right lower lip	Not stated	SK	Single	No (64)
4	55	M	Right forearm	Not stated	VV	Single	No (54)
5	37	M	Right hand	3 mo	SK-irritated, SCC, PN	Single	No (37)
6	31	M	Right thumb	5 y	Digital mucus cyst, PN	Single	No (37)
7	48	M	Right posterior calf	Not stated	SCC	Single	No (20)
8	31	M	Left chest	Not stated	BCC	Single	No (14)
9	74	F	Left anterior thigh	Not stated	AK-hypertrophic, SCC	Single	No (8)
10	68	M	Left buttock	Not stated	Excoriation, psoriasis	Single	No (2)
11	70	M	Forehead	Not stated	AK	Single	No (1)

AK indicates actinic keratosis; BCC, basal cell carcinoma; PN, prurigo nodularis; SCC, squamous cell carcinoma; SK, seborrheic keratosis; VV, verruca vulgaris.

actinic keratosis (3), verruca vulgaris (2), seborrheic keratosis (2), prurigo nodularis (2), basal cell carcinoma (1), digital mucus cyst (1), excoriation (1), and psoriasis (1).

Ten of the 11 specimens were shave biopsies; 1 (case 6) was a punch biopsy. On gross pathologic examination, the specimens ranged in size from $1.6 \times 1.2 \times 0.3$ cm to $0.4 \times 0.3 \times 0.2$ cm, with average dimensions of $0.6 \times 0.5 \times 0.2$ cm.

Microscopically, these were sharply defined lesions with compact orthokeratosis and epidermal acanthosis; some had papillomatosis (Fig. 1). The entire lesion consisted of prominent broad and confluent cornoid lamellae. In addition, there were discrete cornoid lamellae in several different areas of the same lesion (Figs. 2A, B). Prominent dyskeratosis and loss of the granular layer were evident within the cornoid lamellae (Fig. 3). An abrupt transition to normal cornification was seen at the edges (Figs. 4A, B). Superficial dermal changes included mild vascular dilatation with surrounding chronic inflammation (Fig. 4B).

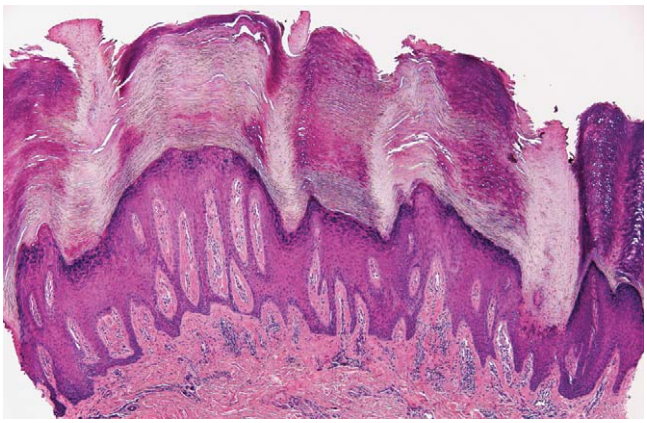

FIGURE 1. Case 6 is characterized by verrucous acanthosis with prominent cornoid lamellae in multiple areas of the same lesion.

Clinical correlation by the treating dermatologists confirmed the absence of a prior diagnosis or family history of porokeratosis. There were no known immunosuppressive conditions or medications associated with any of the patients.

Treatment consisted of complete excision of the lesion in 10 of the 11 cases. In one case where a punch biopsy was taken, cryotherapy was give as the treatment. In all cases, there was no known persistence or regrowth from a persistent lesion after treatment.

DISCUSSION

Cornoid lamellae are microscopically defined by a linear column of parakeratosis which extends in a wavelike fashion through the stratum corneum. The underlying epidermal dyskeratosis and loss of the granular layer are important features that are manifestations of their etiology. Cornoid lamellae are the result of focal abnormal cornification and, as such, create a wake of dyskeratosis along their path resulting in the classic histologic changes. This microscopic feature is observed in a variety of acanthomas and carcinomas; it is not pathognomonic of porokeratosis.[19] Whether they are seen incidentally as a reaction pattern or in porokeratosis, cornoid lamellae are not the solitary feature which defines the lesion.

The cases presented here have a distinct pattern of cornoid lamellation, which is their essential finding. The entire lesion is composed of multiple solitary, as well as broad and confluent, cornoid lamellae. These findings are present throughout the entire lesion, not just at the periphery. There is no central area of epidermal atrophy and no underlying primary disease process. The lesion is well demarcated from the surrounding uninvolved epidermis with an abrupt transition that is easily identified

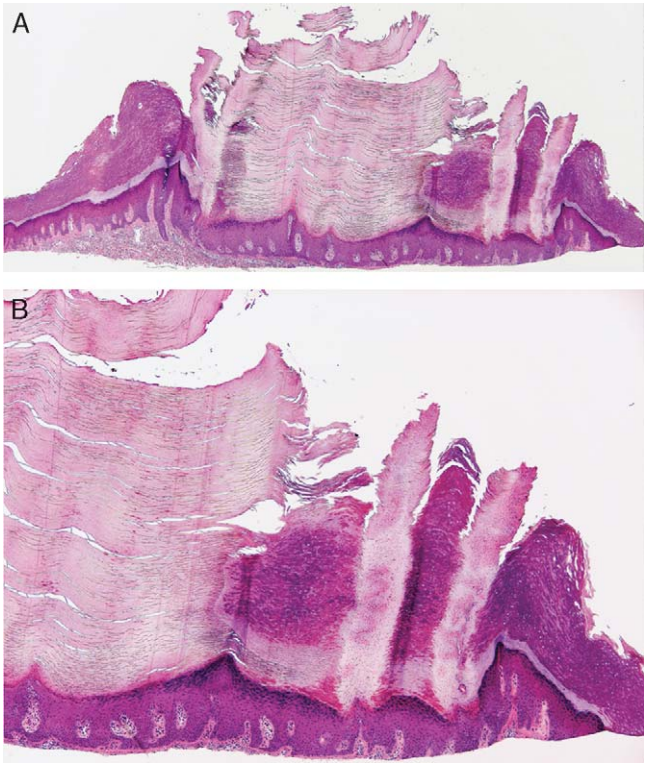

FIGURE 2. A, The low-power architecture in case 5 is characterized by a well demarcated lesion defined entirely by cornoid lamellae, which are arranged in separate and distinct columns as well as a large confluent band. B, At higher magnification, the cornoid lamellae are identified in both the horizontally confluent and isolated, vertically oriented, columnar forms characteristic of this lesion.

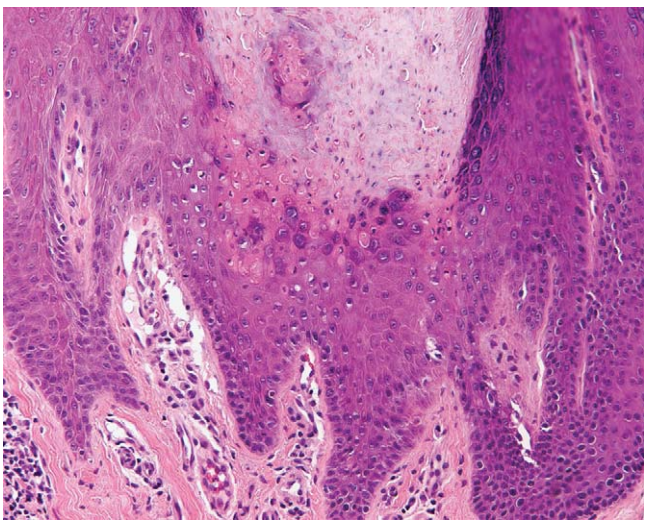

FIGURE 3. A high-power view of case 6 highlights the classic features of the cornoid lamella with a linear ''column'' of parakeratosis that extends in a wavelike fashion through the stratum corneum. Note the underlying prominent dyskeratosis and loss of the granular layer.

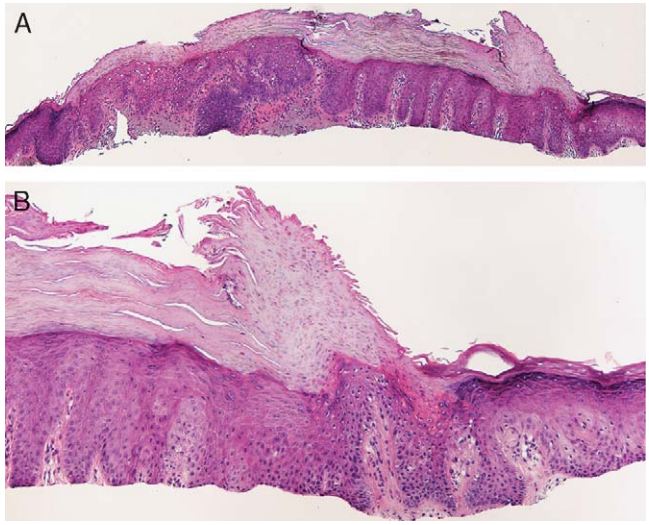

FIGURE 4. A, At low power, the lesion in case 3 is well defined and is composed of one broad, confluent cornoid lamella that is columnar at the periphery. B, This medium-power view highlights the abrupt transition between the lesion and the uninvolved epidermis. There is a distinct cornoid lamella at the interface that transitions into one that is expansive and unified. Changes within the papillary dermis include mild vascular dilatation with a surrounding lymphocytic infiltrate.

on low power. Dermal changes are nonspecific and include mild vascular dilatation with a surrounding chronic inflammatory infiltrate of predominately lymphocytes.

A solitary lesion having a distinctive histologic pattern similar to lesions associated with a generalized disease condition is a recognized phenomenon. It was once thought that the histologic changes seen in bullous congenital ichthyosiform erythroderma were unique and definitive of that disease as proposed by Frost and Van Schott.[7] In their 1966 article, they separated nonbullous congenital ichthyosiform erythroderma from bullous congenital ichthyosiform erythroderma, which they renamed ''epidermolytic hyperkeratosis.''[7,20]

In 1970, Ackerman[1] showed that this alteration in epidermal cornification was a pattern found in both generalized and localized disease, and the term ''epidermolytic hyperkeratosis'' was identified as a pattern in a variety of conditions, not merely a synonym for bullous congenital ichthyosiform erythroderma.[20] Also in 1970, Sharpiro and Baraf[17] described a hyperkeratotic lesion with the classic histology of epidermolytic hyperkeratosis; they identified a solitary tumorlike form that they termed ''epidermolytic acanthoma.'' A similar historic path was taken with the histologic feature of acantholytic dyskeratosis, which was believed to be seen only in Darier and Grover diseases.[5,8] Again, it was Ackerman who, in 1972, proposed the term ''focal acantholytic dyskeratosis'' to separate it as a histologic pattern that was identified in a variety of generalized, localized, solitary, and incidental presentations.[8]

A solitary lesion with the histology of acantholytic dyskeratosis was described and recognized much earlier; it was first called "isolated Darier disease" by Allen in 1954, and then renamed "warty dyskeratoma" in 1957 by Szymanski.[4,18,20]

In a fashion similar, we extend this method of thinking to apply to our current series, the lesions of which have a histology similar to that seen in porokeratosis, but present in a solitary tumorlike form.

In 1974, Ackerman and Goldman[3] described lesions with combined epidermolytic hyperkeratosis and focal acantholytic dyskeratosis. They constructed a table of the clinical variants of epidermolytic hyperkeratosis and focal acantholytic dyskeratosis.[3] We expand on this table by including cornoid lamellation (Table 2).

Although cornoid lamellation integrates our lesion with those of porokeratosis, there are many clinical and histologic features that separate the 2. All of our patients were adults (mean age of 55 y) with the majority being male (M:F = 7:2). Although PPPD and LP can be seen at any age, PM usually occurs in childhood and DSAP and PP occur usually in early adulthood.[21] PM and PPPD have a male predominance, but DSAP is more common in women. LP has an equal sex distribution.[21]

Most lesions of porokeratosis are multiple, although a few variants, namely PM, can be solitary. The lesions of all variants occur most commonly on the extremities with such sites as mucus membranes, trunk, head and neck, and buttocks being affected less frequently.[21] Although our cases of porokeratoma had a similar distribution, mainly on the extremities, they differed in that they were all solitary tumorlike nodules.

The clinical appearance of individual lesions in porokeratosis is characteristic of this disease and is similar in all variants. They are scaling annular plaques that range in size from < 1 to up to 20 cm and have a raised ridgelike hyperkeratotic border with central hypopigmentation and atrophy. DSAP lesions tend to be more discrete, whereas those of PM are more confluent. Porokeratomas range from < 1 cm to nearly 2 cm and are clinically scaling plaques or nodules with central hyperkeratosis. Several in our series had a verrucous appearance.

The differing clinical appearances of the 2 conditions correlate well with their differing histologies. Microscopically, the ridgelike hyperkeratotic borders seen in porokeratosis are due to a single defined cornoid lamella at the lesional edge. The center of the lesion shows epidermal atrophy and foci of basal cell vacuolization. Dermal changes include edema and fibrosis with variable vascular dilatation. In porokeratoma, there is verrucous acanthosis with prominent multiple and confluent cornoid lamellation throughout. Dermal changes are nonspecific and include mild superficial perivascular lymphocytic chronic inflammation. There is no central area of epidermal atrophy or cornoid lamellae present only at the borders; instead, the entire lesion is composed of cornoid lamellation.

Another clinically important distinguishing characteristic between porokeratosis and porokeratoma is established risk factors. PM, DSAP, and PPPD have an autosomal dominant inheritance and an association with immunosuppression.[21] Although suspected, no definitive mode of inheritance has been identified in linear and punctuate forms. Per clinical history and follow-up, none of the patients in our series has a previous diagnosis of any variant of porokeratosis nor any concurrent causes, due either to a disease process or medication, of immunosuppression.

Putative malignant "transformation" (progression?) has been seen with PM, DSAP, PPPD, and, especially, with LP.[10,15] The basal cell carcinomas and squamous cell carcinomas that develop in these variants tend to be more aggressive and, therefore, careful clinical follow-up is

TABLE 2. Clinical Variants of Cornoid Lamellae, Epidermolytic Hyperkeratosis, and Focal Acantholytic Dyskeratosis[3]

Finding ⇒	Cornoid Lamellae	Epidermolytic Hyperkeratosis	Focal Acantholytic Dyskeratosis
Presentation ⇓	Diagnosis ⇓		
Incidental coexistence	AK, SK, scar, VV, milia, SCC in situ, BCC[19]	Intradermal melanocytic nevus, AK, hypertrophic scar, epidermoid cyst, nummular dermatitis, solid hidradenoma[11], pilar cyst, cutaneous horn, SK, lichenoid amyloidosis, GA, SCC[3], epidermal nevi[22]	DF, BCC, chondrodermatitis nodularis helices, comedo, melanocytic nevus, MM[2], linear nevi[22]
Solitary	Porokeratoma	Epidermolytic acanthoma	Warty dyskeratoma
Generalized	Porokeratosis		
Widespread	DSAP, PPPD	Bullous congenital ichthyosiform erythroderma	Darier disease, Grover disease
Systematized	LP, PPPD, PP, PM	PS-1 type[6]	Zosteriform Darier disease

AK indicates actinic (solar) keratosis; BCC, basal cell carcinoma; DF, dermatofibroma; DSAP, disseminated superficial actinic porokeratosis; GA, granuloma annulare; MM, malignant melanoma; PS-1, severe palmoplantar hyperkeratosis, type 1; SCC, squamous cell carcinoma; SK, seborrheic keratosis; VV, verruca vulgaris.

essential. Whether our cases are rudimentary expressions of carcinoma is uncertain, given that all lesions were completely excised or treated with cryotherapy, and no additional or persistent lesions have been identified. In addition, none of our patients had the underlying risk factor of immunosuppression.

Of all the variants of porokeratosis discussed above, the one clinically closest to porokeratoma is PM. Similarities among the 2 include a male predominance and lesion predilection for the extremities. Although PM frequently is seen as multiple, often confluent, lesions, it is the most common variant to be solitary. In addition, PM can present in adults, although it most commonly occurs in children with an autosomal dominant mode of inheritance, and when seen in adults is usually following some form of immunosuppression.

The clinical appearance of the lesions, however, is quite different. PM, like the other variants of porokeratosis, has a distinct raised serpentine outer border with central, often hypopigmented, atrophy. Those of porokeratoma were described clinically as a solitary scaling hyperkeratotic, often verrucous, plaque, or nodule. From the information obtained, porokeratomas seemed to be fairly uniform and did not have a notable outer rim with a differing appearance centrally. In further support of this, porokeratosis of any variant was never listed in the clinical differential diagnoses provided by the treating dermatologists in any of the 11 cases.

The most compelling distinguishing feature between PM and porokeratoma is the histology. PM only has cornoid lamellae present at the periphery, hence the distinct outer border seen clinically. The central portion of the lesion is characterized by epidermal atrophy. In porokeratoma, the lesion is different in that it is entirely made up of cornoid lamellae, both confluent and solitary forms, hence the more uniform appearance clinically. There is neither a separate area of epidermal atrophy nor cornoid lamellae just at the edges. These features are exclusive to porokeratoma and thus separate it out as a distinct entity.

In conclusion, these lesions with a specific pattern of cornoid lamellation appear to be acanthomas with features of porokeratosis, for which we have coined the term *porokeratoma*. Although they share a similar histologic feature of cornoid lamellae, they are clinically and morphologically distinct from porokeratosis and its numerous variants. Because epidermolytic acanthoma and warty dyskeratoma are widely accepted as separate clinicopathologic conditions within a spectrum of histopathologically similar lesions, the same reasoning applies for *porokeratoma*.

REFERENCES

1. Ackerman AB. Histopathologic concept of epidermolyic hyperkeratosis. *Arch Dermatol*. 1970;102:253–259.
2. Ackerman AB. Focal acantholytic dyskeratosis. *Arch Dermatol*. 1972;106:702–706.
3. Ackerman AB, Goldman G. Combined epidermolytic hyperkeratosis and focal acantholytic dyskeratosis. *Arch Dermatol*. 1974; 109:385–386.
4. Allen AC. *The Skin: A Clinicopathologic Treatise*. St Louis: Mosby; 1954.
5. Darier J. Psorospermose folliculaire vegetante. *Ann Dermatol Syphiligr (Paris)*. 1889;10:597.
6. DiGiovanna JJ, Bale SJ. Clinical heterogeneity in epidermolytic hyperkeratosis. *Arch Dermatol*. 1994;130:1026–1035.
7. Frost P, Van Schott EJ. Ichthyosiform dermatosis. *Arch Dermatol*. 1966;94:113.
8. Grover RW. Transient acantholytic dermatosis. *Arch Dermatol*. 1970;101:426–434.
9. Lestringant GG, Berge T. Porokeratosis punctata palmaris et plantaris. A new entity? *Arch Dermatol*. 1989;125:816–819.
10. Magee JW, McCalmont TH, Leboit PE. Overexpression of p53 tumor suppressor protein in porokeratosis. *Arch Dermatol*. 1994; 130:187–190.
11. Mehregan AH. Epidermolytic hyperkeratosis. Incidental findings in the epidermis and in the intraepidermal eccrine sweat duct units. *J Cutan Pathol*. 1978;5:76–80.
12. Mikhail GR, Wertheimer FW. Clinical variants of porokeratosis (Mibelli). *Arch Dermatol*. 1968;98:124–131.
13. Rahbari H, Cordero AA, Mehregan AH. Linear porokeratosis. A distinctive clinical variant of porokeratosis of Mibelli. *Arch Dermatol*. 1974;109:526–528.
14. Rahbari H, Cordero AA, Mehregan AH. Punctate porokeratosis: a clinical variant of porokeratosis of Mibelli. *J Cutan Pathol*. 1977; 4:338–341.
15. Sasson M, Krain AD. Porokeratosis and cutaneous malignancy. A review. *Dermatol Surg*. 1996;22:339–342.
16. Schwarz T, Seiser A, Gschnait F. Disseminated superficial 'actinic' porokeratosis. *J Am Acad Dermatol*. 1984;11:724–730.
17. Sharpiro L, Baraf CS. Isolated epidermolytic acanthoma: a solitary tumor showing granular degeneration. *Arch Dermatol*. 1970;101: 220–223.
18. Szymanski FJ. Warty dyskeratoma. *Arch Dermatol*. 1957;75: 567–572.
19. Wade TR, Ackerman AB. Cornoid lamellation. A histologic reaction pattern. *Am J Dermatopathol*. 1980;2:5–15.
20. Waldo ED, Ackerman AB. Epidermolytic hyperkeratosis and focal acantholytic dyskeratosis: a unified concept. *Pathol Annu*. 1978; 13:149–175.
21. Walff-Schreiner EC. Porokeratosis. In: Freedberg IM, Eisen AZ, Wolff K, et al, eds. *Fitzpatrick's Dermatology in General Medicine*. 6th ed. Vol 1. New York: McGraw-Hill; 2003:532–537.
22. Weedon D. *Skin Pathology*. 2nd ed. London: Churchill Livingston; 2002:292–294.

