

Understanding Porokeratosis

It's easy to confuse this condition with other similar-looking or sounding diagnoses.

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Introduction

During years as a podiatrist in-training and then as a podiatric clinician, I grew increasingly confused regarding the precise nature of many dermatological entities as they involve the lower extremity. My confusion was founded both in apparent inconsistencies with the application of the clinical nomenclature and in what appeared to be unclear or ambiguous definitions for the clinical conditions as they are described in the literature and in academia.

Additional years of training in osteopathy, anatomic pathology, clinical pathology, and oncologic surgical pathology did little to resolve my quandaries. It wasn't until I had the privilege to train in dermatopathology that some of the answers started to become clear, while other answers remained elusive until I was given the opportunity to work in tandem with front-

line clinicians as a podiatric pathologist.

Where is the Confusion?

One of the foremost points of confusion regarded the term "porokeratosis" as it is applied to punctate lesions of the plantar surface. It is clear that even some of my most astute podiatric dermatologists equate intractable plantar keratoses (IPK), porokeratosis punctata, and punctate keratoderma (porokeratosis punctata palmaris et plantaris), spiny keratoderma). I have seen some of our profession's sharpest clinicians use a term "seed wart" to characterize a condition that in most cases is actually punctate keratoderma.

Although these names might sound alike and they may look clinically similar, each of these conditions is actually quite distinct.

From Where Did the Confusion Come?

There are two principle reasons for the confusion revolving around the term "porokeratosis" as it applies to dermatological lesions of the plantar surface.

1) Foremost among them is that due to the combination of the weight-bearing and shearing forces upon the plantar surfaces, and the inherent intrinsic properties of plantar (volar) skin; almost all discrete lesions of the volar surfaces look similar.

Many lesions that might be

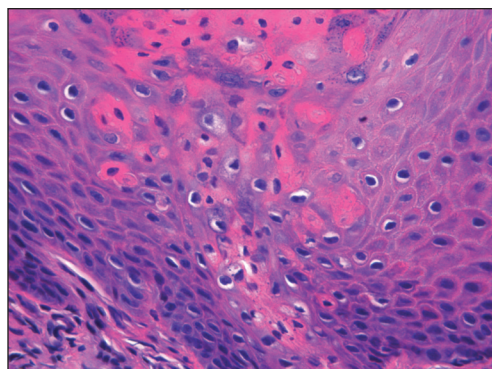


Figure 2: Cornoid lamella. Abnormal dyskeratotic cells at the base of a cornoid lamella.

elsewhere distinguished by their clinical appearance, as they grow exophytically from the skin surface, cannot be so easily told apart on the plantar surface where compressive forces push them into the underlying dermis.

Complicating the clinical findings further is the presence of a thick layer of surface keratin which can further mask the true clinical appearance. The masking effect of the thick plantar keratin can cause well-trained clinicians to misdiagnose plantar melanoma as a "foreign body."

For these reasons, calluses (particularly those beneath metatarsal heads), verrucae, and various neoplasms such as porokeratosis punctata and eccrine poroma may all look essentially identical when arising on weight-bearing surfaces.

2) The second, and possibly most important, contributor to the confusion is that there is an ongoing notion that the aforementioned

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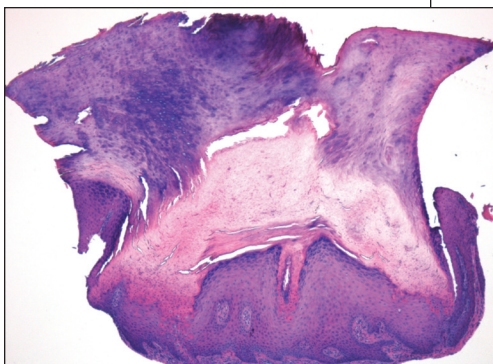


Figure 1: Cornoid lamellae. Opposing columns of porokeratosis project inward from depressions in the surface epithelium.

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Figure 3: Disseminated superficial actinic porokeratosis (DSAP). Note the fine rim of keratin which corresponds to the histopathologic finding of a cornoid lamella. Courtesy A. Bernard Ackerman.

entities are easily distinguished clinically, and thus, these diagnoses are rarely confirmed histopathologically. As a direct result, the same misdiagnoses may be made over and over by clinicians without correction. This lack of histopathologic correlation has contributed toward the perpetuation of many misconceptions.

Such misconceptions begin during our didactic education and, if not corrected, are carried through into our clinical practices. The lack of clinical-histopathologic correlation can also lead to a diminished appreciation for the clinical appearances of numerous other neoplasms or dermatitides.

There are yet other contributing factors to this confusion. There is a plethora of overlapping nomenclature regarding discrete lesions of



Figure 4: Porokeratosis of Mibelli. Irregular annular lesion with central atrophy and ulceration. The prominent rim is formed by a large corned lamella. Courtesy Patrick Campbell, DPM

the plantar surface, much of which is largely inappropriate. For example, “poro” implies a relationship with the sweat apparatus, yet in the overwhelming majority of cases of porokeratosis, no such relationship exists.

The term “porokeratosis plan-taris discreta”, as coined by the late Doctor Steinberg¹ was probably less than ideal because intractable plantar keratoses (IPK) have nothing to do with the sweat apparatus and, rather, are purely a biomechanical phenomenon. This point has been previously made in the podiatric literature.² IPKs are also entirely unrelated to genuine porokeratosis in that the latter are small clonal (neoplastic) proliferations that arise independent of external trauma.³ From a histopathologic vantage point, IPKs do not display cornoid lamellation, which bona-fide porokeratosis do.

Further confusing the nomenclature is the term “porokeratosis punctata”, which is often inappropriately equated with punctate keratoderma of the palms and soles. In the overwhelming majority of cases, individual lesions in punctate keratoderma do not exhibit cornoid lamellae. In addition, punctate keratoderma seems to have a distinct epidemiology and lacks the association with squamous cell carcinoma that is seen in association with true porokeratosis variants. Punctate keratoderma is surely the more appropriate term for cases with diffuse involvement of the volar surfaces by small 1-3 mm. keratotic pits that do not possess cornoid lamellation.

In contrast to the many misnomers that have been perpetuated for lesions of the plantar surface, the designation “eccrine poroma” seems to be more appropriate in that it denotes a neoplasm that is comprised of cells that actually do exhibit eccrine (and/or apocrine) differentiation.

So What Actually are Porokeratoses?

Porokeratoses are small



Figure 5a: Porokeratosis punctata. Ill-defined peripheral rim of keratin with a histopathologically distinguishable cornoid lamella.



Figure 5b: Porokeratosis punctata-porokeratosis of Mibelli crossover lesion. The overwhelming majority of the bona-fide cases of plantar porokeratosis that we see in our practice are not small and punctate, but rather have features reminiscent of small porokeratosis of Mibelli.

clonal proliferations of keratinizing squamous cells.^{3,4} Clonality implies that the cells that make up the lesion are derived from a common “mother cell”. All neoplasms, both benign and malignant, exhibit clonality. The fundamental pathogenesis of such clonal tumors involves the development of a sequence of genetic mutations that first lead to cellular immortality and then to uninhibited growth. Benign neoplasms simply acquire the ability to grow autonomously, while malignant neoplasms further gain the ability to invade adjacent tissues and/or metastasize.

Porokeratoses of all types are defined histopathologically by a

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structure called a cornoid lamella⁵. Cornoid lamellae are columns of parakeratotic keratin that overlie a depression within the surface epithelium (Figure 1). Cells at the base of the cornoid lamella exhibit abnormal keratinization (Figure 2). Porokeratoses may demonstrate any of several distinct patterns of growth. Each of these patterns has a distinct clinical appearance, which may be used to classify such lesions as a particular porokeratosis variant, e.g., linear, punctate, Mibella, disseminated, etc.

Variants of Porokeratosis

There are several clinical variants of porokeratosis. The most common form of porokeratosis is disseminated superficial actinic porokeratosis (DSAP) (Figure 3). This variant presents in the third to fourth decade of life as small 3-5mm. pruritic flat-topped papules. With progression, each individual lesion expands radially, becoming centrally atrophic. The cornoid lamellae are seen clinically as a thin ring of hyperkeratosis encircling peripherally around each lesion. In most cases, DSAP presents with widespread lesions affecting the extremities bilaterally, but sparing the palms and soles.^{6,7} There is often an autosomal dominant pattern of inheritance.^{6,7}

Porokeratosis of Mibelli (Figure 4) is also a relatively common variant of porokeratosis that is usually solitary and may occur on any cutaneous or mucosal surface; however, the extremities are most commonly affected.⁸ These lesions begin quite small but expand centrifugally to become variably large in diameter. Occasional cases may become massive and exhibit locally destructive behavior. Ulceration is not uncommon in aggressive cases. Like DSAP, porokeratosis of Mibelli may manifest in association with immuno-suppression and in rare instances, it may be seen in association with squamous cell carcinoma.⁹

Apart from porokeratosis of Mibelli, the porokeratosis variant that is most important to clinicians of the lower extremity is

porokeratosis punctata (punctate porokeratosis) (Figure 5). Unfortunately, this form of porokeratosis is poorly understood and inadequately studied. Inhibiting our understanding of this condition is the fact that clinicians, and even many textbooks, still equate porokeratosis punctata with punctate keratoderma (Figure 6). This is despite the fact that punctate keratoderma lack cornoid lamellation, which a requisite to be classified

as a true porokeratoses variant (Figure 7).

In some instances, probably due to the confusing nature of the nomenclature, podiatric physicians equate intractable plantar keratosis (porokeratosis plantaris discreta) with porokeratosis punctata. Further inhibiting our understanding of this uncommon porokeratosis variant is deep palmo-plantar wart (myrmecia), which

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represents a major diagnostic pitfall due to its occasional lack of a verrucous configuration and pinpoint bleeding upon debridement. The lack of histopathologic sampling with plantar lesions, particularly in the research arena, has further accentuated the confusion pertaining to this variant of porokeratosis.



Figure 6: Punctate keratoderma. Although often lumped with porokeratosis, the lack of cornoid lamellation precludes such a diagnosis. Courtesy Sean Van Marter, DPM

Punctate Porokeratosis

Punctate porokeratosis presents itself as one or more discrete punctate lesions on the palms or soles. In our experience, porokeratosis punctata (PP) is exceedingly rare, representing a tiny percentage of lesions clinically believed to be porokeratoses, which at some point undergo confirmational biopsy. They begin as small seed-like keratinized papules, each with a peripheral raised rim on the palms and soles.¹⁰ Lesions may be bilateral or unilateral.^{11,12}

In our experience, the diffuse 1-3 mm. keratotic plugs, which are widely described as porokeratosis punctata, are almost uniformly punctate (non-porokeratotic) keratoderma. True porokeratoses from the sole nearly always resemble either small porokeratosis of Mibelli-like lesions (Figure 8), or porokeratoses of the ver-

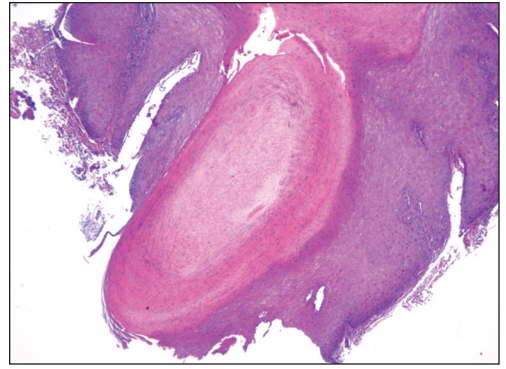


Figure 7: Punctate keratoderma. Punch biopsy specimen taken for a case of punctate keratoderma showing a discrete keratotic plug without porokeratosis or dyskeratosis. Sean Van Marter, DPM

rucous subtype.

The punctate form of porokeratosis is believed to be somewhat distinct among porokeratosis variants. This is due to the absence of a known association with squamous cell carcinoma; however, we believe that this claim cannot be completely substantiated. Because a histopathologic diagnosis is rarely

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obtained for porokeratosis-like lesions of the weight-bearing surfaces, known genuine porokeratoses are virtually never followed for extended periods of time to assess for the eventual development of squamous cell carcinoma.

As previously noted, in our experience, the overwhelming majori-

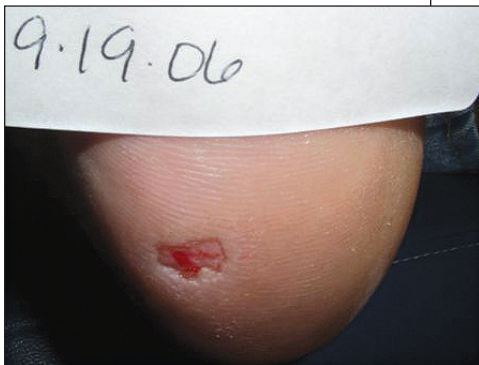


Figure 8: Porokeratosis involving the skin of the heel. This porokeratosis more closely resembles a small porokeratosis of Mibelli than it does punctate porokeratosis. Courtesy Christina Weber, DPM.

ty of cases of *presumed* porokeratosis punctata are in actuality alternate benign or reactive lesions that are known to have no association with carcinoma. Parenthetically, we have seen plantar squamous cell carcinoma, which upon excision, exhibited focal features suggestive of an associated porokeratosis.

Other Variants

Other porokeratosis variants that deserve mention are linear porokeratosis and verrucous porokeratosis. Linear porokeratosis is most notable for its close association with squamous cell carcinoma.¹³ Due to the tendency for the verrucous variant to become markedly hyperkeratotic, thereby mimicking verruca vulgaris, and because it may arise on the lower extremity (including the plantar surface), clinicians should be aware of its existence.¹⁴ Many of the genuine plantar porokeratoses that we see in our practice have features of

the verrucous variant.

Differential Diagnosis

The differential diagnosis for porokeratosis punctata was previously alluded to. Virtually any discrete lesion of the plantar surface may be considered within its differential diagnosis, most notably: deep palmoplantar wart (Figure 9), IPK (Figure 10), and punctate keratoderma. Porokeratosis of Mibelli may be confused with a spectrum of conditions depending on its size, degree of keratinization, and presence of ulceration. Prominent within its differential diagnosis are granuloma annulare and squamous cell carcinoma.

Management of Porokeratosis Variants

Just as porokeratosis punctata is, in many respects, poorly characterized as an entity, studies addressing the treatment options for this particular variant of porokeratosis are almost entirely lacking in the litera-

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Figure 9: Deep palmoplantar wart. The lack of pinpoint bleeding upon debridement is often misleading to treating clinicians.

porokeratosis of Mibelli involve immunomodulation to prompt destruction of the lesion in question through mechanisms relating to the host immune system.

Treatments that have been shown to be effective in

ture. From a theoretical perspective, the most important point in the treatment of porokeratoses is that they are neoplasms, and thus will continue to grow autonomously unless their constituent cells are completely destroyed or excised. The newest strategies in the treatment of

the treatment of porokeratosis of Mibelli and DSAP include imiquimod 5% cream, 5-fluorouracil, retinoids (tretinoin, isotretinoin), pulsed dye laser, cryosurgery, and excision.¹⁵⁻²⁰ It is likely that similar treatments would be effective for histopathological-

ly confirmed cases of porokeratosis punctata. To potentiate such treatments for porokeratosis punctata, clinicians might consider the concurrent use of either salicylic acid or a high concentration urea-based keratolytic, possibly under occlusion.

Punctate keratoderma (porokeratosis punctata palmaris et plantaris, spiny keratoderma) do not enlarge and are largely asymptomatic unless arising over a bony prominence. Therefore, treatment is limited to symptomatic lesions and consists of palliative measures. Both porokeratoses and symptomatic lesions in punctate keratoderma may be excised. Individual symptomatic lesions in punctate keratoderma may be removed with small punch biopsies, taking care to remove the keratotic plug while minimizing deep dermal and subcutaneous extension to limit associated scar formation. ■



Figure 10: Intractable plantar keratosis. Often larger than punctate porokeratoses, without significant inflammation, and uniformly seen on weight bearing surfaces beneath bony prominences. Courtesy Chad Webster, DPM.

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