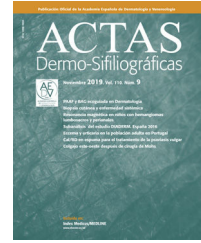




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CARTA CIENTÍFICO-CLÍNICA

[Translated article] Seborrhuca: Vindication of a Pattern?

Seborrhuca: ¿reivindicación de un patrón?

To the Editor,

Scientific medical literature, sometimes, describes seborrheic keratosis (SK) as a seborrheic wart due to its clinical similarity to warts. However, microscopic examination is a significant tool to distinguish between these 2 entities.

There are several morphological types of SK recognized in the literature, being the acanthotic and reticulated types the most common of all. In addition to these, we would like to highlight a pattern we frequently encounter in our routine dermatopathology practice that, still, has not been described in the classic texts on SK: the coexistence within the same lesion of overlapping features of SK and a common wart. We have coined the term “seborrhuca” to describe this pattern.

Seborrhuca exhibit characteristics of common warts: a papillomatous silhouette (fig. 1A), hyperkeratosis, columns of parakeratosis at the tips of the papillae (fig. 1B) with agranulosis underneath the parakeratotic column and a prominent granular layer in some other regions (fig. 1C). In the papillary dermis of the papillae, tortuous and often dilated capillaries become evident (fig. 1D). Focal koilocytic changes can sometimes be seen (fig. 1E). Many different characteristics of SK overlapping these wart-typical features are, also, evident. Excessive growth of monomorphic round cells, for example, is prominent (fig. 1F). Additionally, corneal pseudocysts or infundibular tunnels can sometimes be an accompanying feature, as well as the typical whorls of SK (fig. 2B).

Whether this type of SK is related to human papillomavirus (HPV) infection is still a matter of discussion. Studies on HPV associated with SK have included all types of SK without morphological selection of the seborrhuca type. Therefore, most of the cases included probably fall into the category of acanthotic SK. For example, Lee et al. studied a total of 40 non-genital SKs by polymerase chain reaction (PCR) and found no HPV of the types tested.¹ However, their figure 1A—selected by them as representative of their series—clearly shows an acanthotic type of SK.¹

Conversely, other studies have managed to find HPV in SK: HPV-like particles in ultrastructural studies of non-genital SK;² HPV DNA detected in 20% of non-genital SKs by in situ hybridization;³ and 15% up to 30% of SK cases positive for HPV on the PCR.⁴

In the cases found in the genital area, the association with HPV infection seems even stronger, with the virus demonstrated in up to 72% of genital cases by PCR or immunohistochemistry⁴ to the point that some authors claim that genital SKs containing HPV are actually condylomas acuminata.^{1,5}

In this regard, Zhu et al. presented a very interesting study of DNA amplification by PCR in lesions they called “benign verrucous acanthomas,” describing them with characteristic features of common warts but lacking koilocytes in the granular layer.⁶ They could not find any HPV DNA sequences in amplified samples of these benign verrucous acanthomas⁶ but found HPV in verrucous lesions with koilocytes. Consequently, they considered koilocytes as the critical histopathological sign distinguishing common warts from benign verrucous acanthoma.⁶ Admitting this, however, would grant koilocytes a specificity and sensitivity as high as HPV-PCR, which contrasts with what has been described in the scientific medical literature on this

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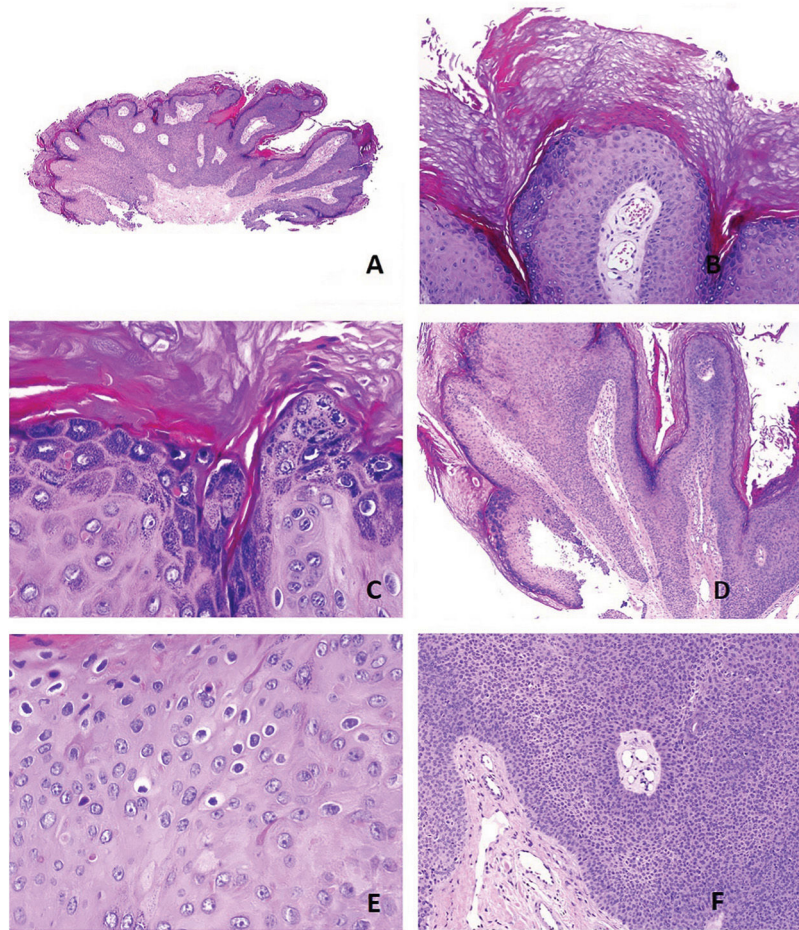


Figure 1 Histopathological features observed in seborrhea: A) papillomatous silhouette (H&E x20). B) parakeratotic columns at the tips of the papillae with agranulosis (H&E x100). C) thick keratohyalin granules (H&E x200). D) tortuous capillary vessels in the papillae (H&E x100). E) koilocytes (H&E x400). F) overgrowth of monomorphic basaloid cells (H&E x100).

67 regard. For example, in a very comprehensive study on
68 histopathological features and HPV types, Jablonska et al.
69 confirmed the presence of koilocytes only in warts induced
70 by certain viral types (such as HPV-4 or HPV-10) but not in
71 others.⁷ As we know, HPV-4 and HPV-10 are related to flat
72 warts, while common warts are usually caused by HPV-2⁸
73 and condylomas by HPV-6 and HPV-11⁹ (types 6 and 11 can
74 also be found in common warts in adults⁹). Other HPV types
75 sometimes found in common warts are HPV-16, 42, 43, or
76 44.⁹

77 **Figure 2** shows additional examples of seborrucas at low
78 magnification. But how significant is seborrhea then? Is it
79 a viral verrucous change (related to HPV) overlapping a
80 SK, that is, a common wart-like SK? Or is it a seborrheic
81 change occurring in a common wart, that is, a common wart-
82 like SK? Or is it the collision of a SK and a common wart?
83 Or is it merely a morphological change mimicking a wart
84 but without the HPV infection? We'd rather stick to option
#1 for 3 reasons: in the first place, common wart changes

sometimes collide with SK areas (fig. 3A); also, when HPV is
studied in collision cases, it is only seen in verrucous—not
in SK—regions.¹⁰

Therefore, we conducted several immunohistochemical
studies with Ki67 and p16 in seborrhea cases, and results
are similar to those seen in a viral warts, i.e., patchy groups
of more than 10 cells positive for p16 (fig. 3B and C), with
a high proliferation index in the basal layers of the lesion
(fig. 3D). This contrasts with what has been reported in
SK cases (negative for p16) (fig. 3E). Furthermore, these
findings contrast with what has been confirmed through
evidence in obvious collision cases between common warts
and seborrheic keratosis, in which only the common wart
areas test positive for p16, while the seborrheic keratosis
test negative for p16 (fig. 3F and G). All these findings sup-
port the idea that seborrhea is a lesion with morphological
characteristics of seborrheic keratosis that has sustained
an HPV infection, eventually leading to the acquisition of
additional wart-like features.

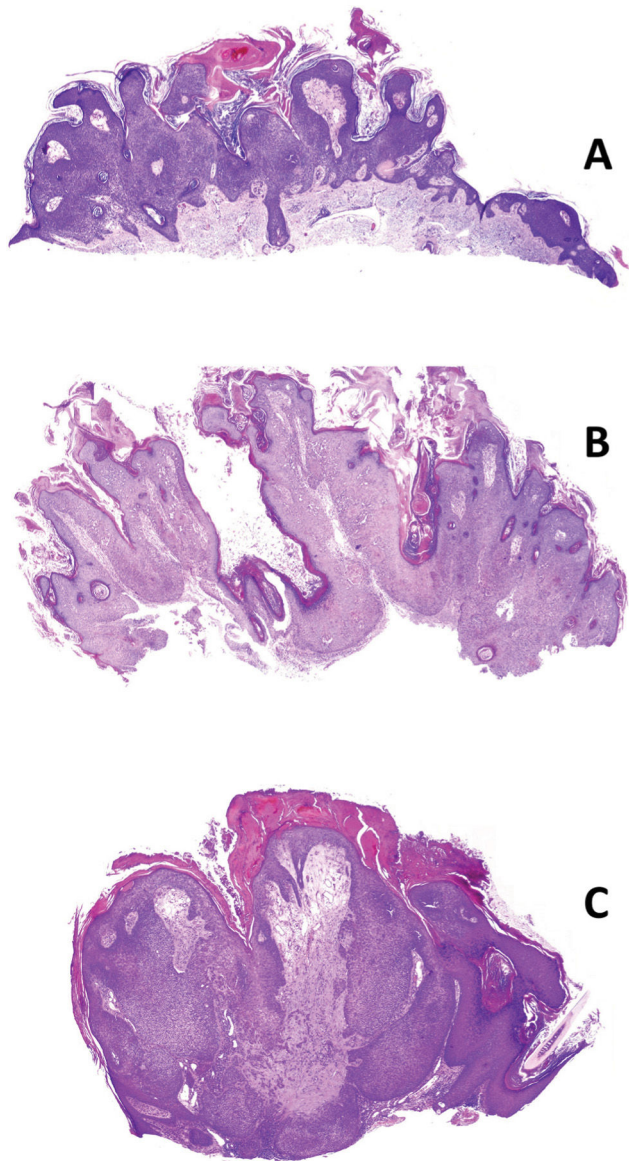


Figure 2 Three examples of seborrucas showing typical features commonly shared by warts and SK (H&E x20). Many whorls can be seen in B.

103 The term seborruca is intended for cases in which
104 histopathological features overlap so much that a simple
105 diagnosis of wart or SK would be arbitrary. It is not intended
106 to replace either of those diagnoses when the morphological
107 features are clear enough to the point of being able to
108 achieve a specific diagnosis of one of these entities.
109

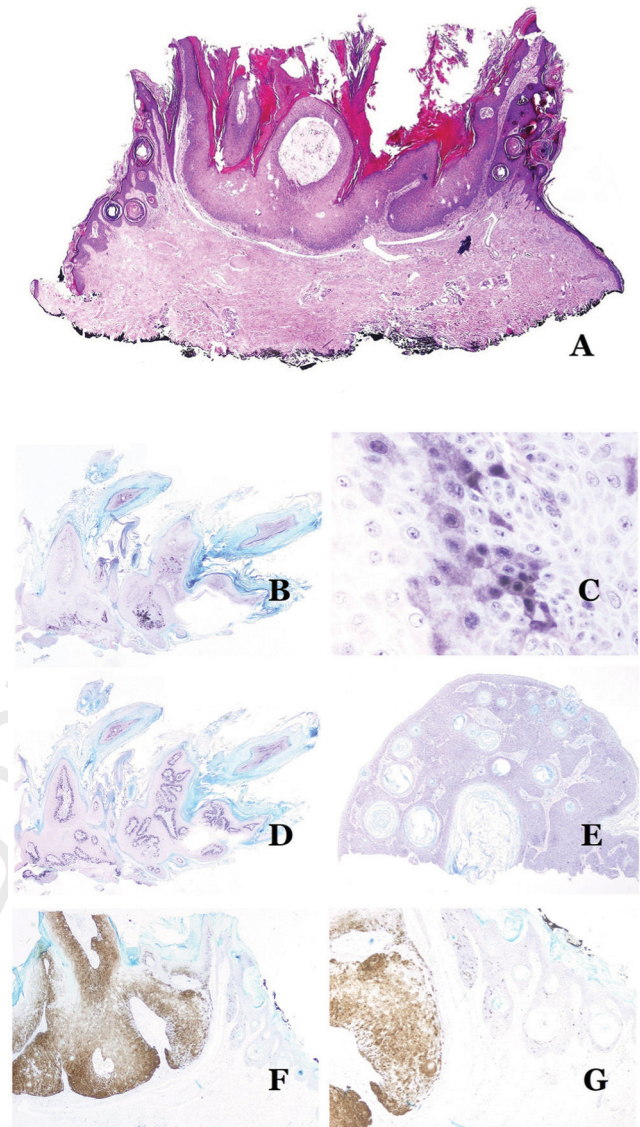


Figure 3 A) Changes of common wart in collision with peripheral areas of SK (H&E x20). B, C, and D) Typical features of seborruca in the immunohistochemical study. Seborruca shows patches of positive staining with p16 (B: p16, x20). The patches consist of more than 10 cells positive for p16, with both cytoplasmic and nuclear staining (C: p16, x400). Ki-67 shows positivity in the basal layer of the lesion only (D: Ki67, x20). In contrast, SK is p16 negative (E: p16, x20). When collision lesions between wart and SK are seen, the wart areas are p16-positive while the SK ones are p16-negative (F: p16, x20; G: p16 x40).

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