Verrucoid Lesion on the Eyelid

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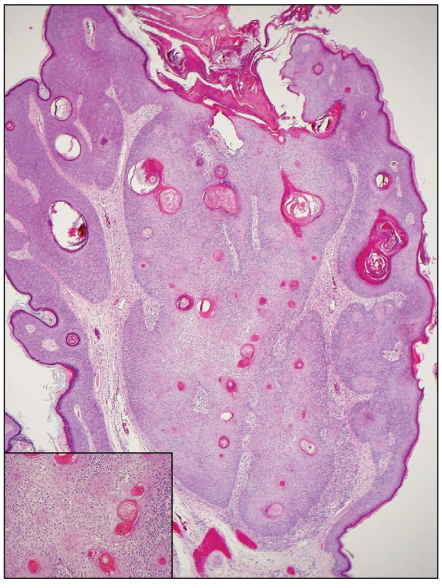

H&E, original magnification ×20 (inset, original magnification ×200).

A 60-year-old man presented with a 3-mm verrucous papule on the right upper eyelid of 2 years' duration.

THE BEST **DIAGNOSIS IS:**

a. acantholytic squamous cell carcinoma
b. desmoplastic trichilemmoma
c. inverted follicular keratosis
d. pilar sheath acanthoma
e. warty dyskeratoma

PLEASE TURN TO PAGE 227 FOR THE DIAGNOSIS

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The authors report no conflict of interest.
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THE **DIAGNOSIS:** Inverted Follicular Keratosis

The differential diagnosis for endophytic squamous neoplasms encompasses benign and malignant entities. The histologic findings of our patient's lesion were compatible with the diagnosis of inverted follicular keratosis (IFK), a benign neoplasm that usually presents as a keratotic papule on the head or neck. Histologically, IFK is characterized by an endophytic growth pattern with squamous eddies (quiz images). Inverted follicular keratosis may represent an irritated seborrheic keratosis or a distinct neoplasm derived from the infundibular portion of the hair follicle; the exact etiology is uncertain.[1,2] No relationship between IFK and human papillomavirus (HPV) has been established.[3] Inverted follicular keratosis can mimic squamous cell carcinoma (SCC). Important clues to the diagnosis of IFK are the presence of squamous eddies and the lack of squamous pearls or cytologic atypia.[4] Squamous eddies consist of whorled keratinocytes without keratinization or atypia. Superficial shave biopsies may fail to demonstrate the characteristic well-circumscribed architecture and may lead to an erroneous diagnosis.

Acantholytic SCC is characterized by atypical keratinocytes that have lost cohesive properties, resulting in acantholysis (Figure 1).[5] This histologic variant was once categorized as an aggressive variant of SCC, but studies have failed to support this assertion.[5,6] Acantholytic SCC has a discohesive nature producing a pseudoglandular appearance sometimes mistaken for adenosquamous carcinoma or metastatic carcinoma. Recent literature has suggested that acantholytic SCCs, similar to IFKs, are derived from the follicular infundibulum.[5,6] Also similar to IFKs, acantholytic SCCs often are located on the face. The invasive architecture and atypical cytology of acantholytic SCCs can differentiate them from IFKs. Acantholytic SCCs can contain keratin pearls with concentric keratinocytes showing incomplete keratinization centrally, often with retained nuclei, but rare to no squamous eddies unless irritated.

Trichilemmoma is an endophytic benign neoplasm derived from the outer sheath of the pilosebaceous follicle characterized by lobules of clear cells hanging from the epidermis.[7] A study investigating the relationship between HPV and trichilemmomas failed to definitively detect HPV in trichilemmomas and this relationship remains unclear.[8] Desmoplastic trichilemmoma is a subtype histologically characterized by jagged islands of epithelial cells separated by dense pink stroma and encased in a glassy basement membrane (Figure 2). The presence of desmoplasia and a jagged growth pattern can mimic invasive SCC, but the absence of cytologic atypia and the surrounding basement membrane differs from SCC.[4,7] Trichilemmomas typically are solitary, but multiple lesions are associated with Cowden syndrome. Cowden syndrome is a rare autosomal-dominant condition characterized by the presence of benign hamartomas and a predisposition to the development of malignancies including breast, endometrial, and thyroid cancers.[9,10] There is no such association with desmoplastic trichilemmomas.[11]

Pilar sheath acanthoma is a benign neoplasm that clinically presents as a solitary flesh-colored nodule with a central pore containing keratin.[12] Histologically, pilar

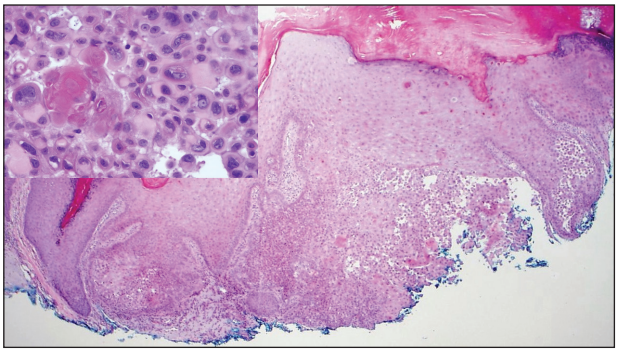

FIGURE 1. Acantholytic squamous cell carcinoma showing keratin pearl and atypia (H&E, original magnification ×40 [inset, original magnification ×600]).

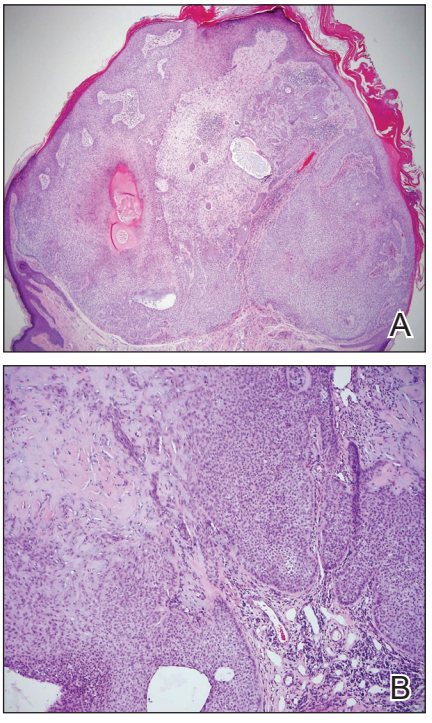

FIGURE 2. Desmoplastic trichilemmomas (A)(H&E, original magnification ×40) with a smooth outline, clear cells, and central jagged islands in a dense pink stroma (B)(H&E, original magnification ×100).

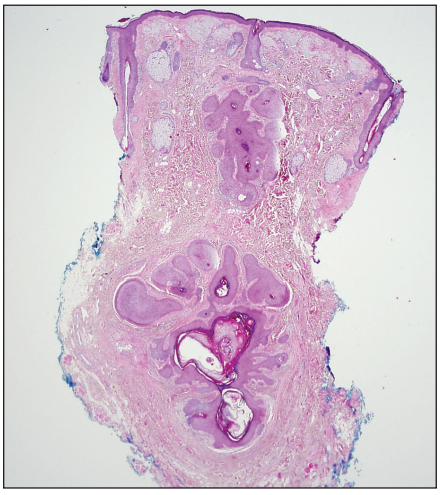

FIGURE 3. Pilar sheath acanthoma with acanthotic epidermal projections (H&E, original magnification ×20).

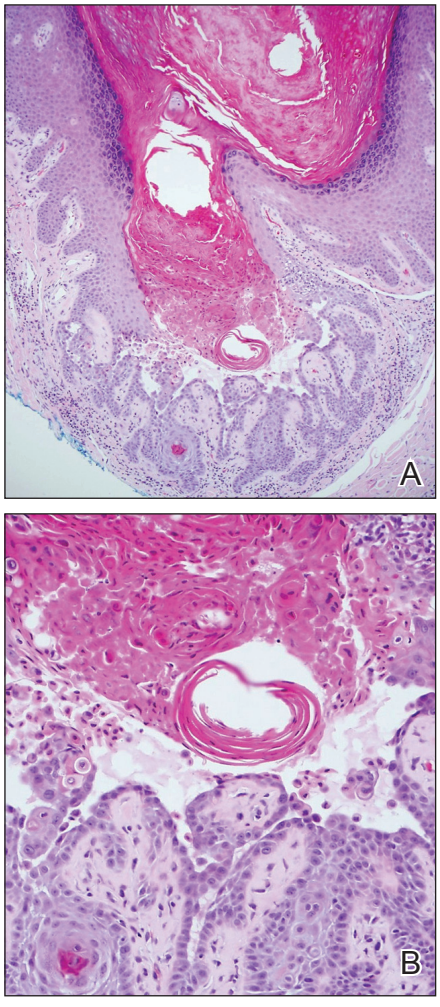

FIGURE 4. Warty dyskeratoma (A)(H&E, original magnification ×100) showing acantholytic dyskeratosis (B)(H&E, original magnification ×200).

sheath acanthoma is similar to a dilated pore of Winer with the addition of acanthotic epidermal projections (Figure 3).

Warty dyskeratoma (WD) is a benign endophytic neoplasm traditionally seen as a solitary lesion histologically similar to Darier disease. Warty dyskeratomas are known to occur both on the skin and oral mucosa.[13] Histologically, WD is characterized as a cup-shaped lesion with numerous villi at the base of the lesion along with acantholysis and dyskeratosis (Figure 4). The dyskeratotic cells in WD consist of corps ronds, which are cells with abundant pink cytoplasm, and small nuclei along with grains, which are flattened basophilic cells. These dyskeratotic cells help differentiate WD from IFK. Although they are endophytic neoplasms, WDs are well circumscribed and should not be confused with SCC. Despite this entity's name and histologic similarity to verrucae, no relationship with HPV has been established.[14]

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