CHAPTER 1
Epidermis

CHAPTER MENU

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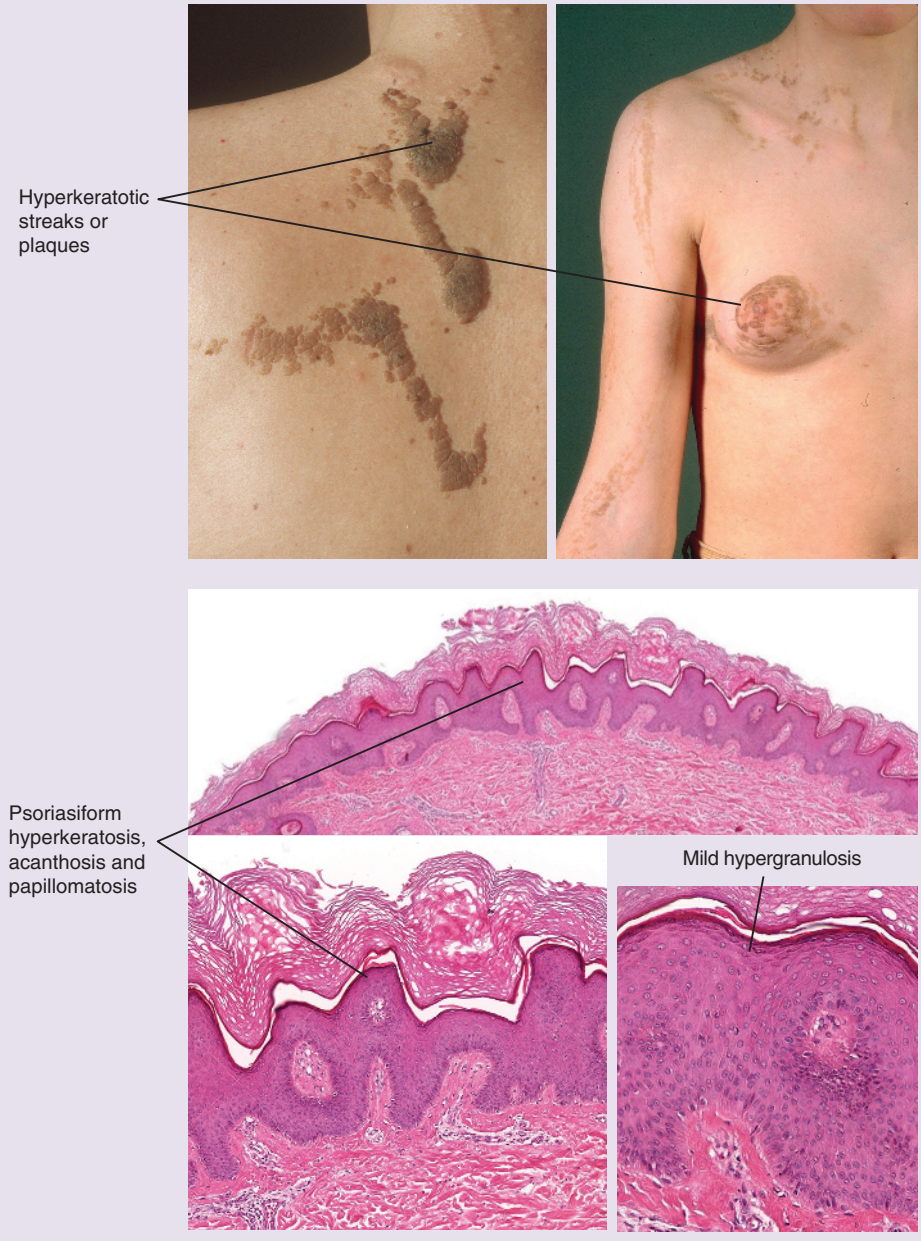
Nevi

Epidermal Nevus



Cl: Epidermal nevi are the most common manifestations of cutaneous mosaicism. They are autosomal dominant segmental hyperkeratotic verrucous or papular lesions present at birth. They present as brown or gray isolated, linear, zosteriform, or whorled patches or follow Blaschko lines.

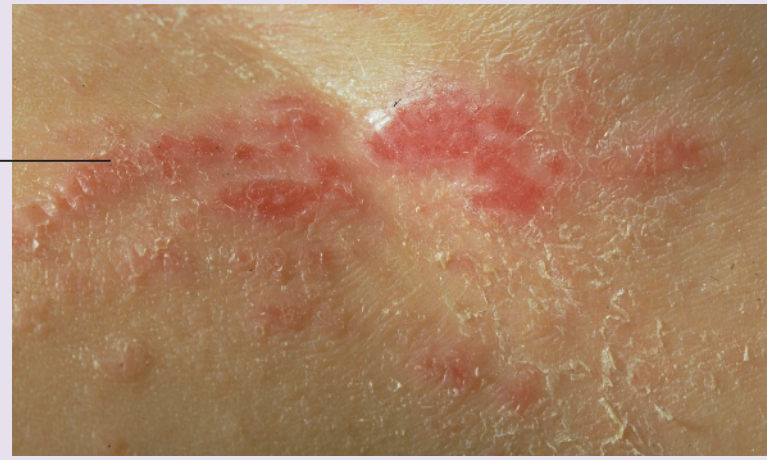
Hi: Psoriasiform acanthosis, papillomatosis, orthohyperkeratosis.

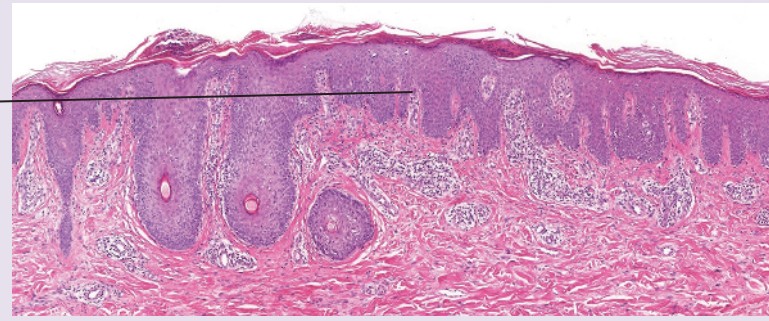
DD: Seborrheic keratosis; epidermolytic hyperkeratosis.

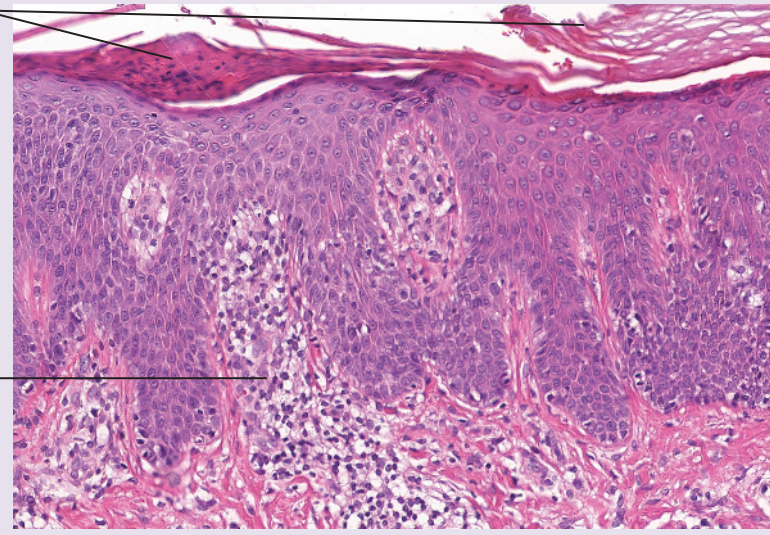
Reference

Chi, C.C., Wang, S.H., and Lin, P.Y. (2009) Combined epidermal-connective tissue nevus of proteoglycan (a type of mucinous nevus): a case report and literature review. *J Cutan Pathol* **36**(7): 808–11.

Variant: Inflammatory Linear Verrucous Epidermal Nevus (ILVEN)







SEBORRHEIC KERATOSIS AND VARIANTS

Cl: ILVEN is considered a variant of epidermal nevus. It shows linear verrucous streaks with inflammatory erythema, scaling, and pruritus.
Hi:

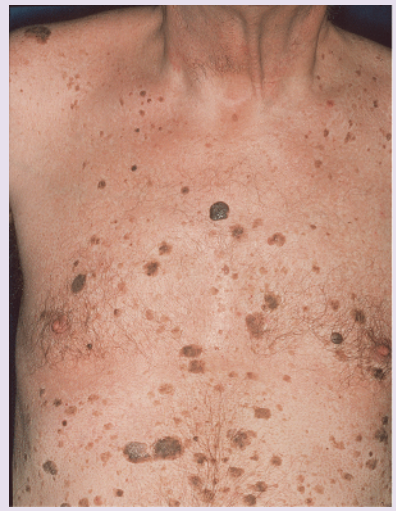
- Psoriasiform acanthosis and papillomatosis
- Alternating areas of ortho- and parakeratosis
- Decreased to absent granular layer
- Prominent acantholysis in some cases
- Inflammatory infiltrate in the papillary dermis

Keratoses

Seborrheic Keratosis (SK) and Variants

Most common epidermal tumor. Synonyms: Senile keratosis, seborrheic wart. Even though resembling common warts, there is no association with human papilloma virus (HPV). They are benign but cosmetically disturbing, sometimes irritated, and occasionally are confused with pigmented tumors like malignant melanoma or pigmented basal cell carcinoma.
Cl: Seborrheic keratosis may present various clinical features. The most common variants are *acanthotic seborrheic keratoses*, which occur as multiple elevated light or dark brown lesions of various sizes preferentially on the trunk, head, and neck of elderly people, sparing palms and soles. *Flat seborrheic keratoses* are referred to as solar lentigo in sun-exposed areas. Others are *papillomatous* and hyperkeratotic with a ceribriform surface. They may be inflamed (*irritated* or "activated"). *Melanoacanthoma* is a dark pigmented seborrheic keratosis in elderly people, which may be confused with malignant melanoma**.** *Dermatosis papulosa nigra*, preferentially occurring in the suborbital and temporal region of black and dark-skinned individuals, presents as tiny pigmented papules. *Reticulated adenoid* (pigmented) and *clonal* (intraepidermal, Borst–Jadassohn) seborrheic keratosis or SK with "*monster cells*" are distinct histological features without special clinical presentation. Hyperkeratotic SK (*stucco keratoses*) appear as tiny multiple whitish hyperkeratotic lesions like gypsum splatters on the dorsum of hands, feet, and lower legs.
DD: Verruca vulgaris; acrokeratosis verruciformis (Hopf).

Variant: Acanthotic Seborrheic Keratosis

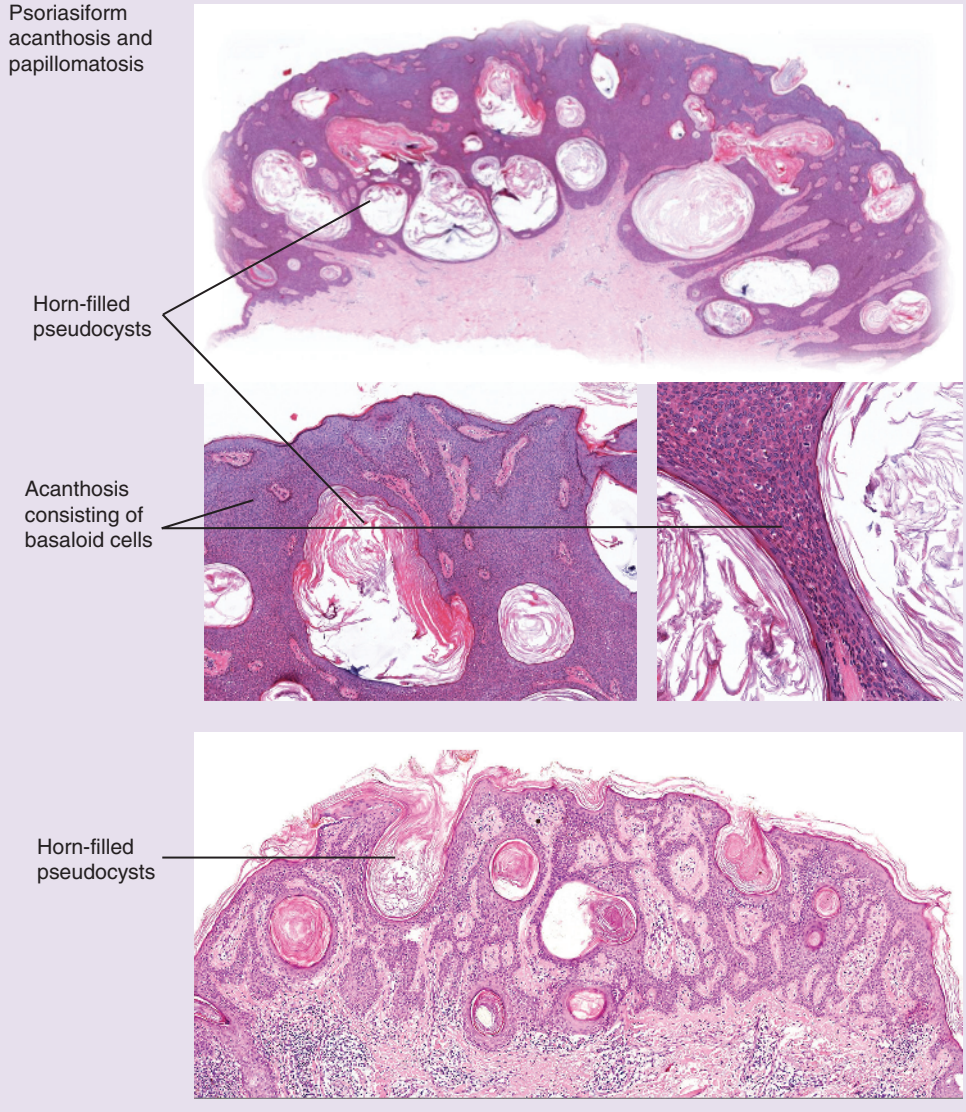


Multiple seborrheic keratoses on the trunk

Flat (above) and papillomatous (below) seborrheic keratoses

SEBORRHEIC KERATOSIS AND VARIANTS

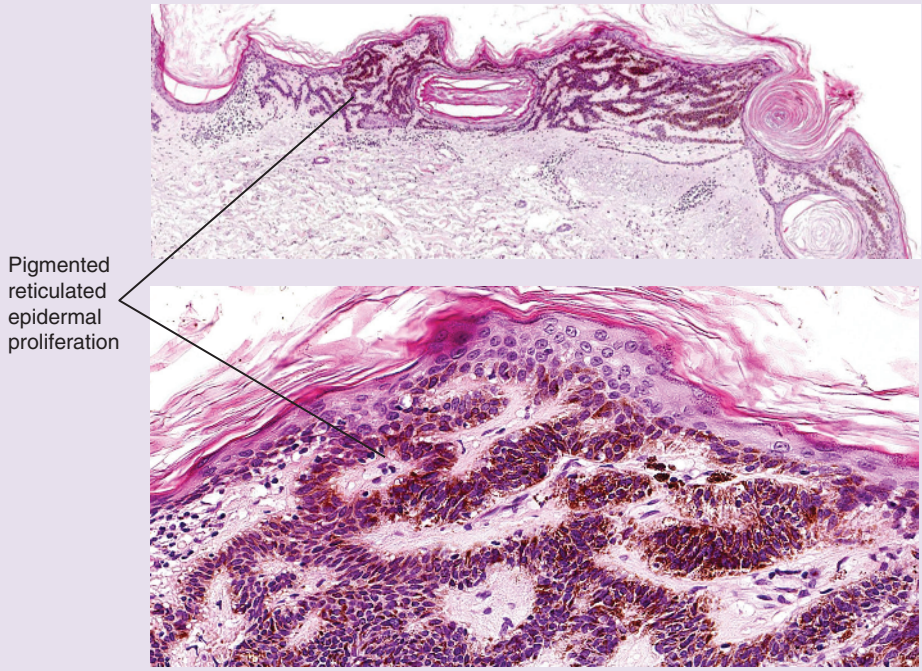
Variant: Acanthotic Seborrheic Keratosis



Hi: Broad acanthotic epidermis composed of basaloid cells. Anastomosing horny pseudocysts filled with keratin.

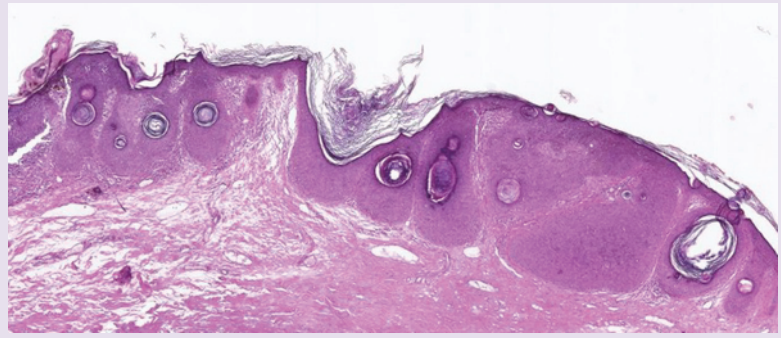
SEBORRHEIC KERATOSIS AND VARIANTS

Variant: Reticulated, Pigmented Seborrheic Keratosis



Hi: Anastomosing small epithelial cords mostly with basal pigmentation forming a reticular net.

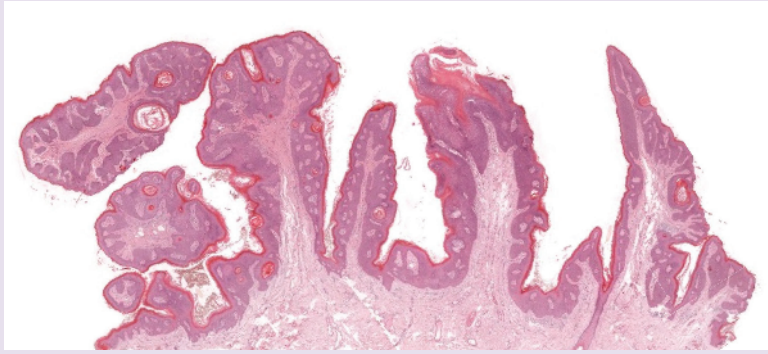
Variant: Flat Seborrheic Keratosis



Hi: Flat plump acanthosis with keratin-filled horny pseudocysts.

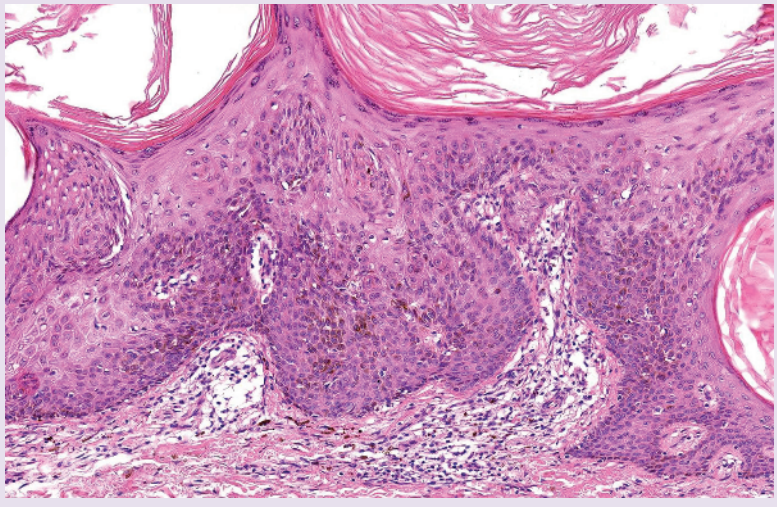
SEBORRHEIC KERATOSIS AND VARIANTS

Variant: Papillomatous Seborrheic Keratosis



Hi:
- Church spire-like proliferations
- Papillomatosis
- Ortho- and parakeratosis

Variant: Activated (Irritated) Seborrheic Keratosis



Hi: Mixed cellular inflammatory infiltrate in the upper dermis and between rete ridges.

Variant: Dermatosis Papulosa Nigra

Cl: Multiple tiny black papules in almost 50% of black-skinned individuals, commonly located on the cheeks and periorbital region. They resemble small seborrheic keratosis.

Hi: Corresponds to flat or reticulated pigmented seborrheic keratosis.

DD: Small seborrheic keratosis; fibromas.

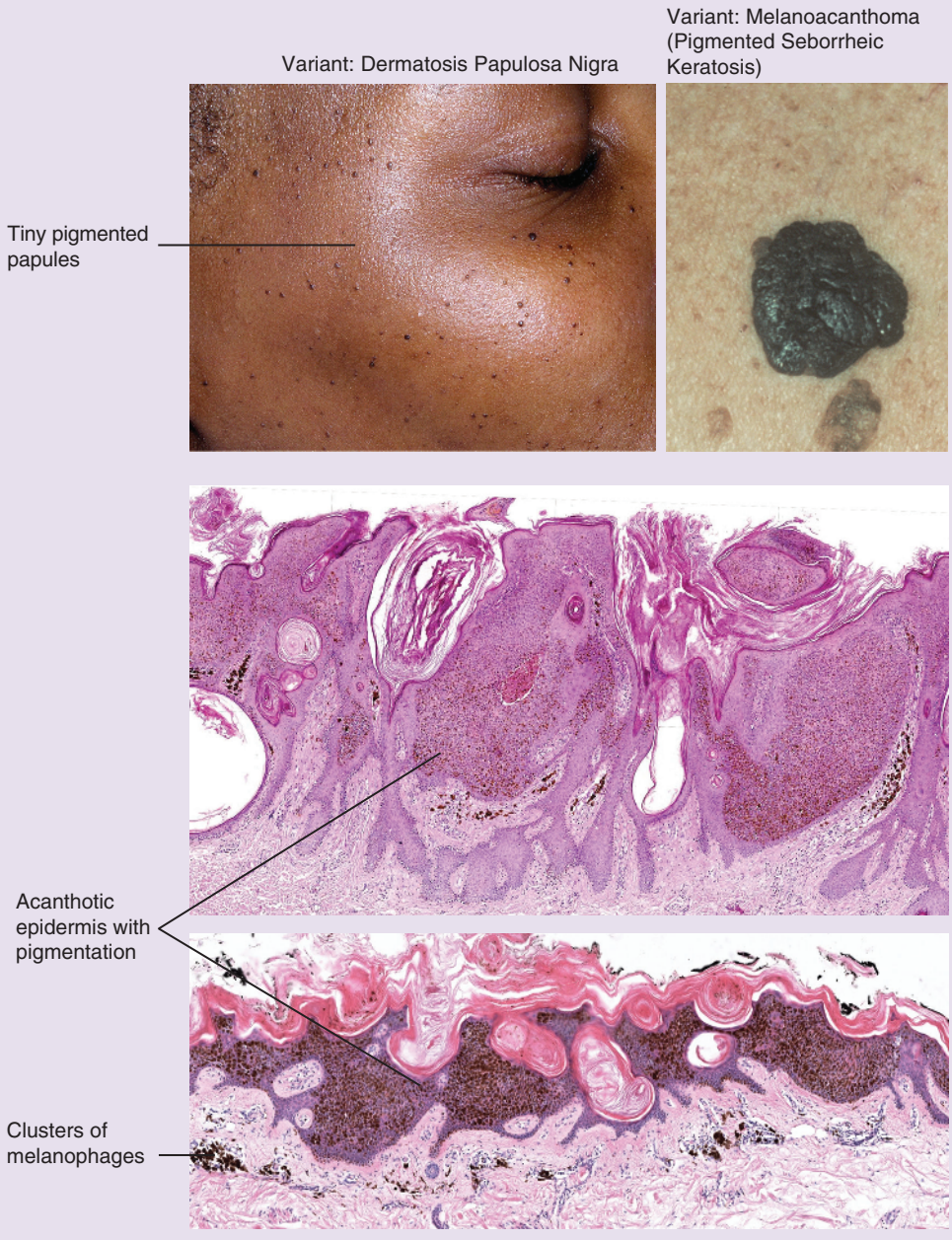
Reference

Grimes, P.E., Arora, S., Minus, H.R., and Kenney, J.A. Jr (1983) Dermatosis papulosa nigra. *Cutis* **32**(4)L 385–6, 392.

SEBORRHEIC KERATOSIS AND VARIANTS

Variant: Dermatosis Papulosa Nigra

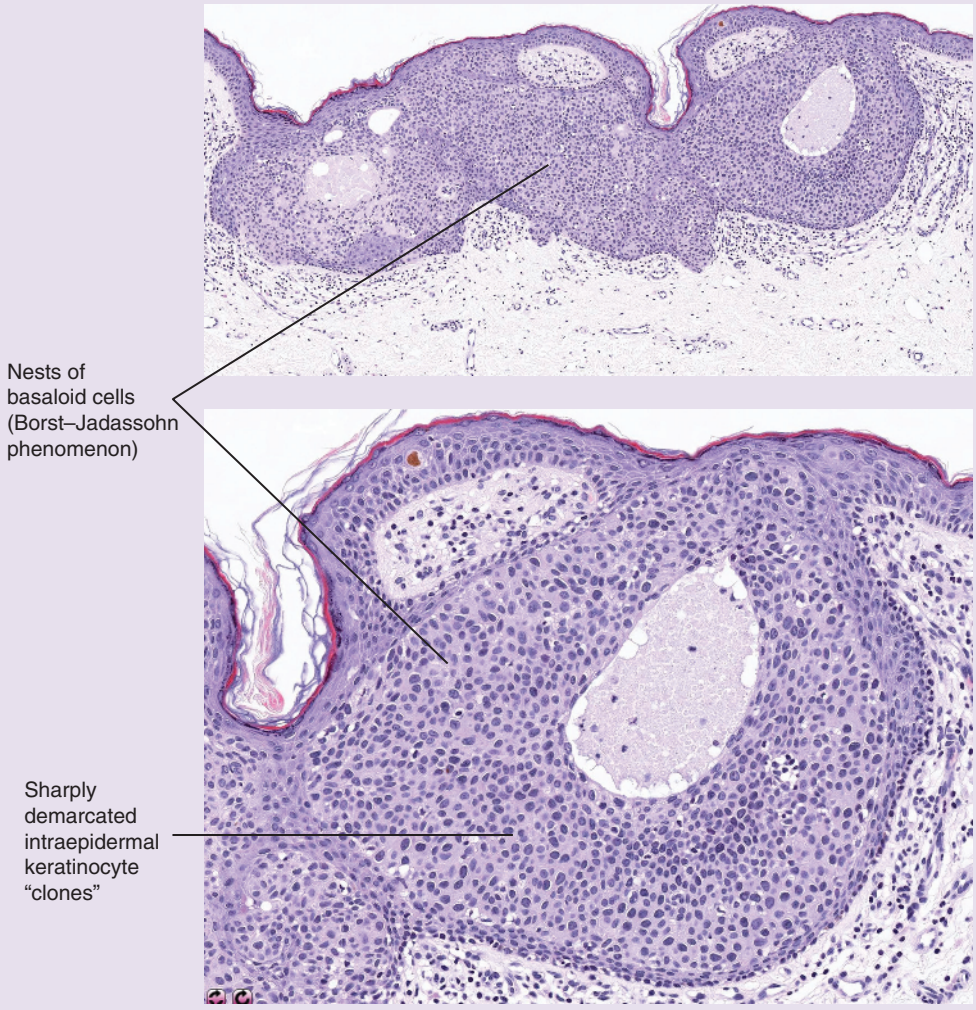
Variant: Melanoacanthoma (Pigmented Seborrheic Keratosis)



Hi: Deeply pigmented variant of acanthotic seborrheric keratosis, consisting of a mixture of pigmented keratinocytes and dendritic melanocytes.

SEBORRHEIC KERATOSIS AND VARIANTS

Variant: Clonal (Intraepidermal) Seborrheic Keratosis (Borst–Jadassohn)



Hi: Intraepidermal clonal accumulation of epidermal cells, sometimes demarcated by stronger pigmentation.

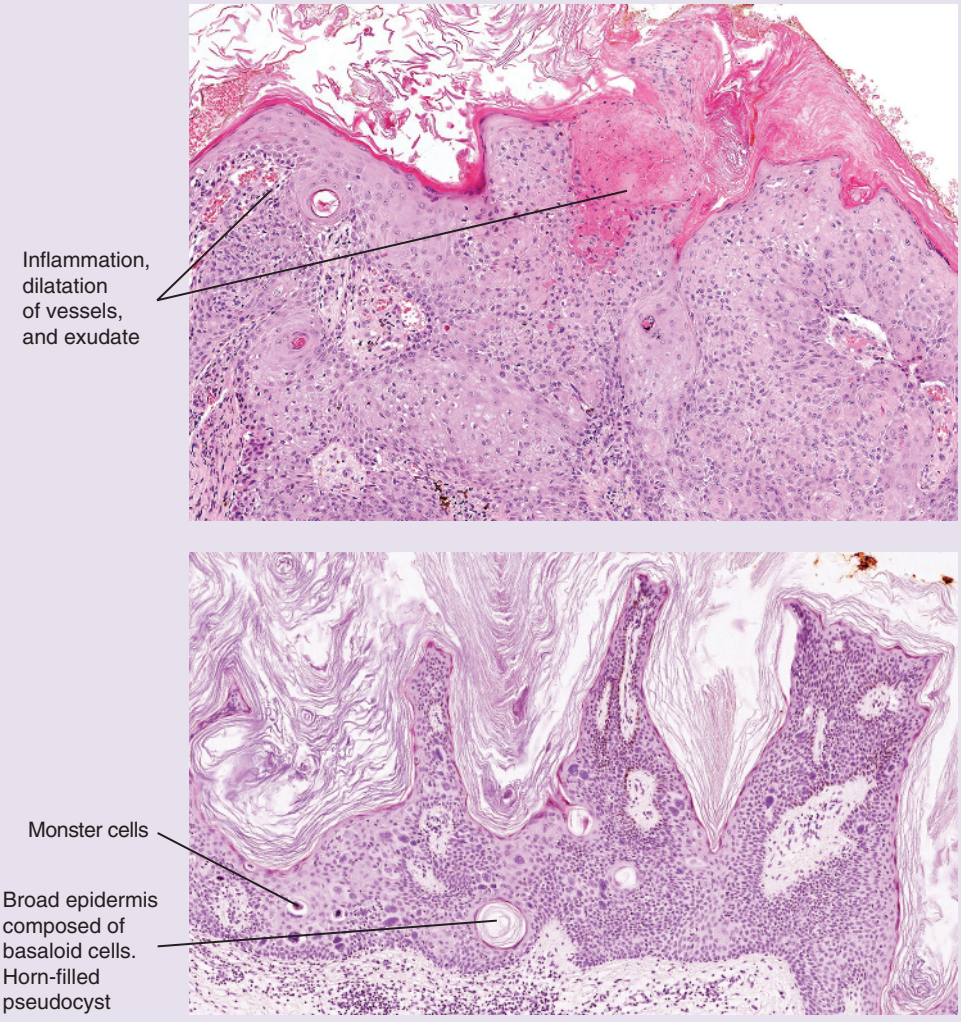
DD: Hidroacanthoma simplex (eccrine poroma); clonal Bowen disease; intraepidermal squamous cell carcinoma.

Reference

Lora, V., Chouvet, B., and Kanitakis, J. (2011) The "intraepidermal epithelioma" revisited: immunohistochemical study of the Borst-Jadassohn phenomenon. *Am J Dermatopathol* **33**(5): 492–497.

SEBORRHEIC KERATOSIS AND VARIANTS

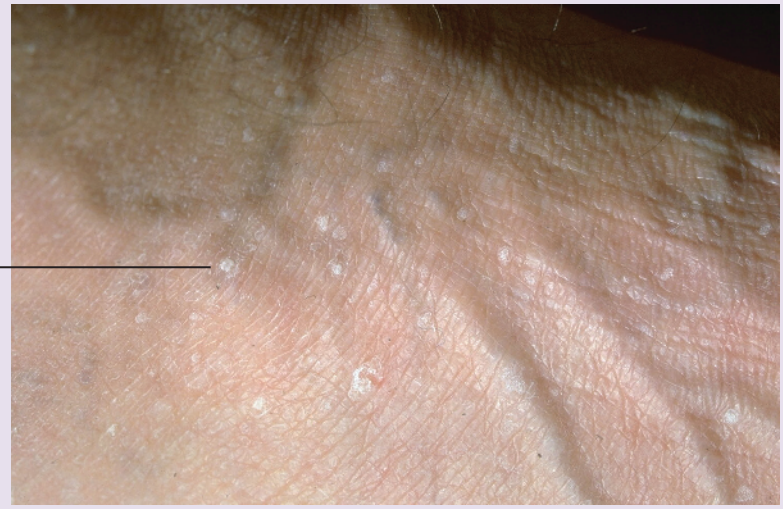
Variant: Seborrheic Keratosis with Monster Cells (Bowenoid)

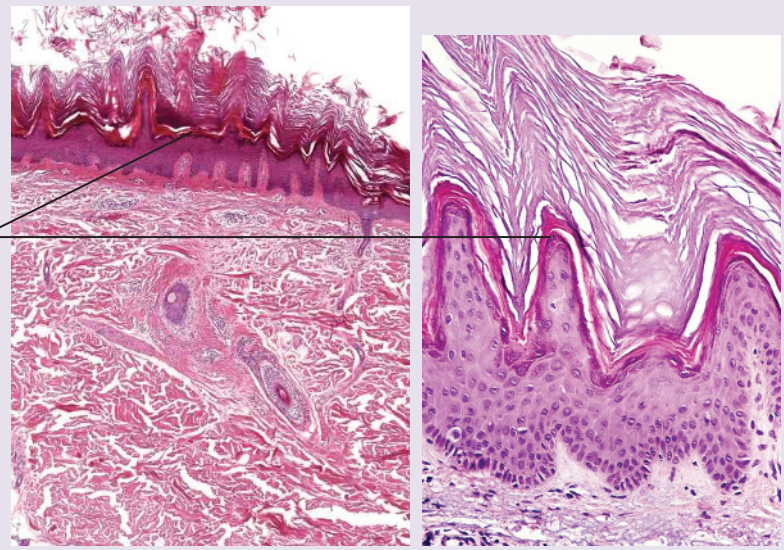


Hi: Morphological variant of SK with scattered large, haloed cells.

SEBORRHEIC KERATOSIS AND VARIANTS

Variant: Hyperkeratotic Seborrheic Keratosis (Stucco Keratosis)

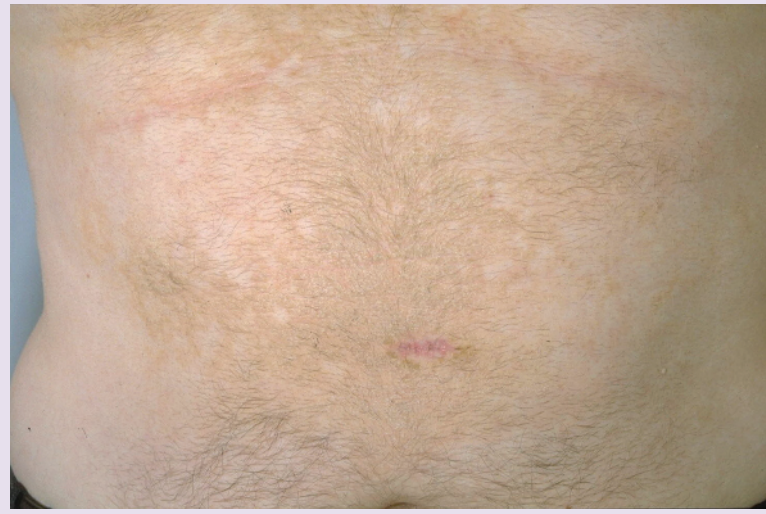




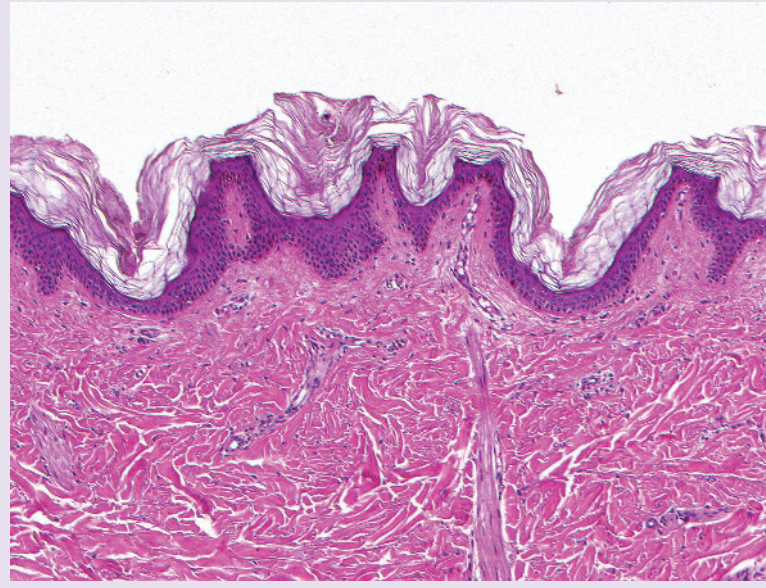
Hi: Acanthosis and orthohyperkeratotic spikes.

Confluent and Reticulate Papillomatosis (Gougerot and Carteaud)

Confluent and reticulated brownish patches resembling pityriasis versicolor



Hyperkeratosis and slight acanthosis; no inflammation

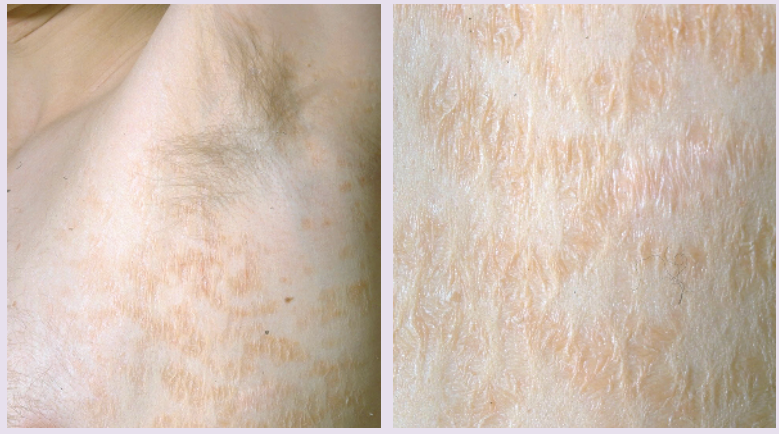


Cl: Gray-brown tiny asymptomatic papules, similar to seborrheic keratosis, coalescing to larger plaques or reticular net, resembling pityriasis versicolor or acanthosis nigricans. Sternum and back are the favorite localisations.

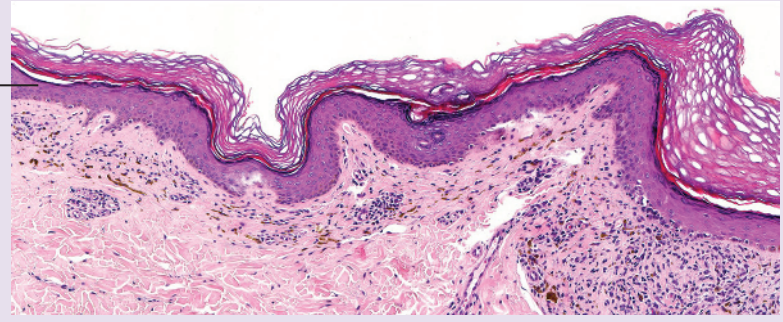
Hi: Slight papillomatosis and hyperkeratosis resembling acanthosis nigricans. Often colonization with *Pityrosporon (Malassezia) orbiculare* (PAS stain).

Reticulate Pigmented Anomaly of the Flexures (Dowling–Degos Disease)

Reticulate hyperpigmentation on the lateral side of the chest



Slight atrophy

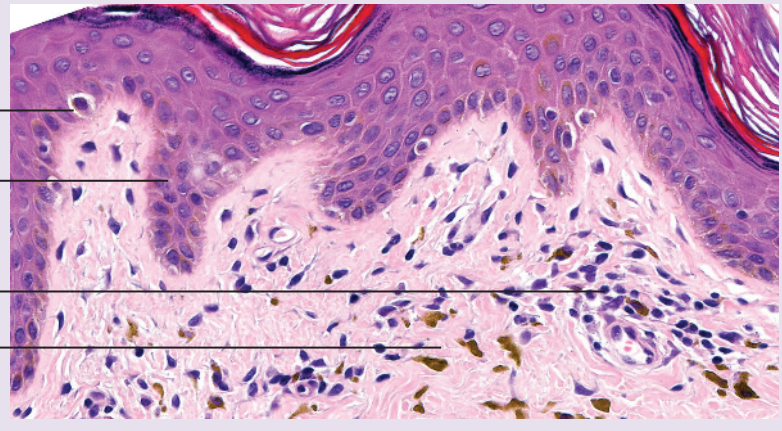


Melanocyte

Downward projection of rete ridges

Slight inflammation

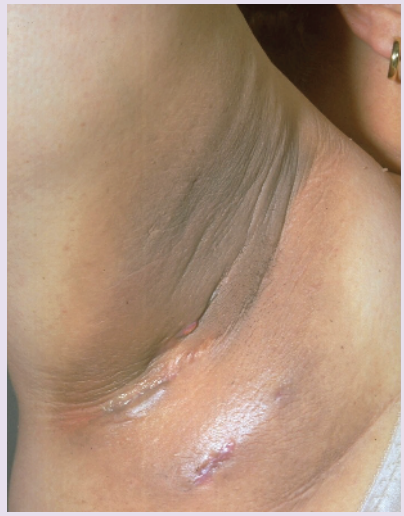
Melanophages loaded with pigment

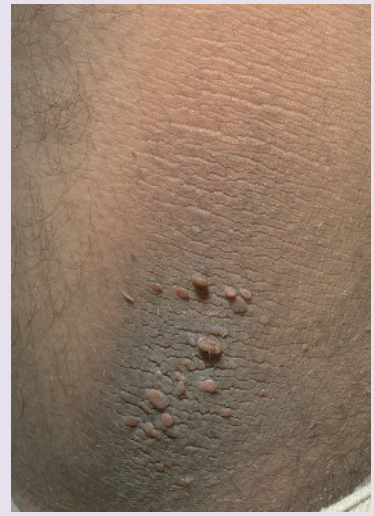


Cl: Congenital, autosomal dominant inherited disease (mutation in the keratin 5-gene *KRT5*), manifesting mostly in adults. Symmetrical small brown macules, resulting in reticular hyperpigmentation of flexural areas (cubital and popliteal fossae, axillae, lateral aspects of the neck, groins).

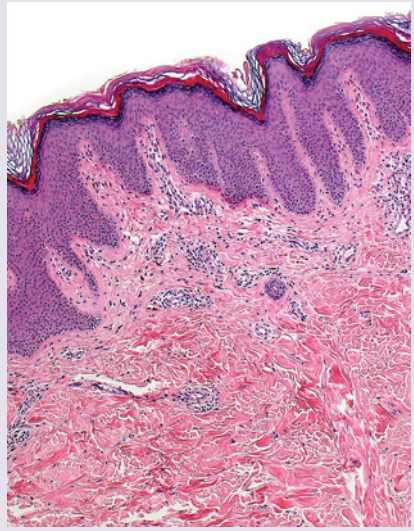
Hi: Similar to flat seborrheic keratosis with basal hyperpigmentation; normal number of melanocytes. Downward projection of the epidermal rete ridges.

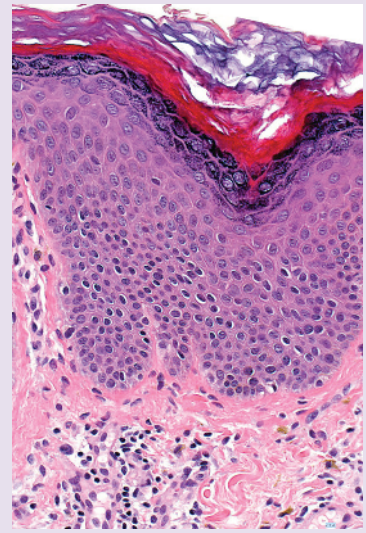
Acanthosis Nigricans





Gray-brown verruciform papules and crests





Alternate ortho- and parahyperkeratosis, acanthosis, papillomatosis (left)

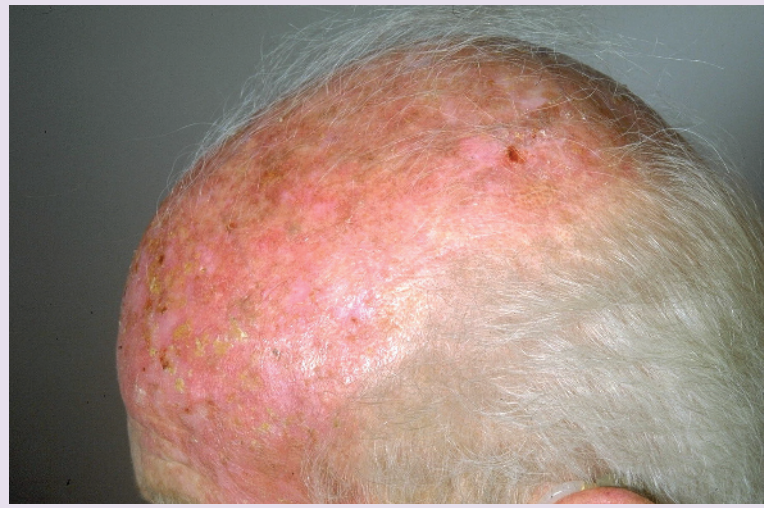
Morphological variant with marked hypergranulosis (right)

Cl: Gray-brown verruciform papules in major intertriginous and flexural areas or neck. The skin shows a velvety surface with crests. It may be associated with a variety of underlying disorders, including obesity (pseudo-acanthosis nigricans benigna), congenital syndromes, hormonal disorders, or malignancies as a paraneoplastic process (acanthosis nigricans maligna).

Hi:
- Alternate ortho- and parahyperkeratosis
- Acanthosis
- Papillomatosis
- Little or no basal layer hyperpigmentation

DD: Acrochordon; small seborrheic keratosis; epidermal nevus.

Solar (Actinic) Keratosis

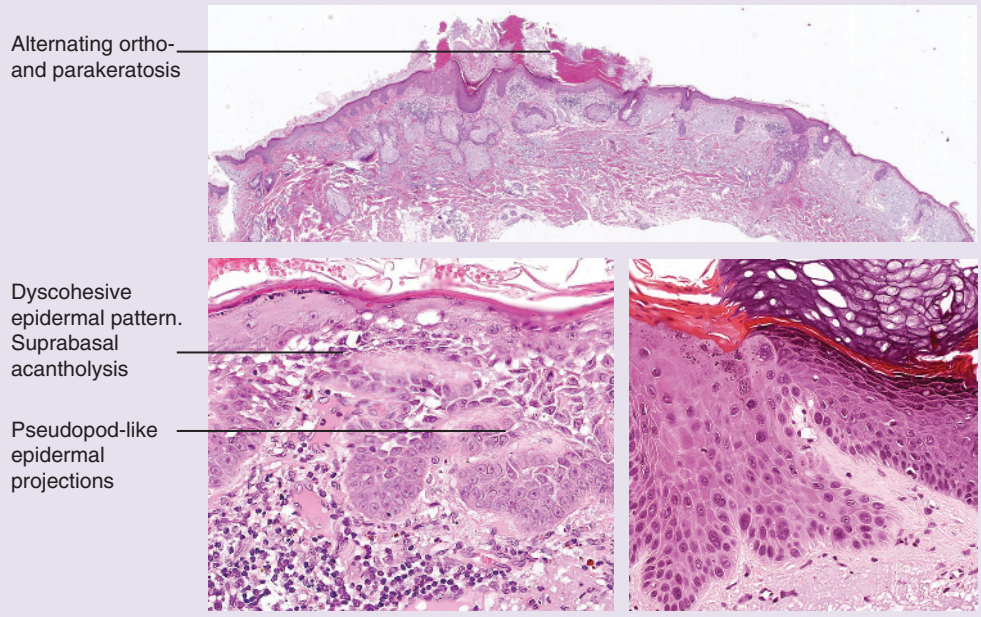


Multiple solar (actinic) keratoses on the scalp

Cl: Actinic keratoses are considered by some to be squamous cell carcinomas *in situ*. However, from a prognostic point of view, they are nosologically different.They are induced by chronic (sunlight) UV exposure and therefore the most common locations are the face, especially nose and ears, and back of the hands and the scalp of bald-headed men. Several variants exist: hypertrophic, bowenoid, atrophic, lichenoid, pigmented. The development of a cutaneous horn, bleeding with hemorrhagic crust, may simulate squamous cell carcinoma or should raise suspicion of malignant transition into squamous cell carcinoma.

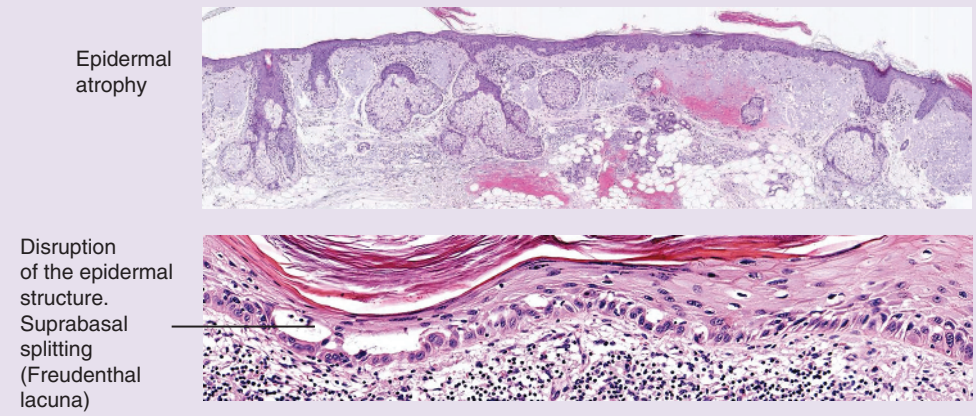
Hi:
- Many different histological patterns may be seen, reflecting the great clinical variability
- Focal areas of orthohyperkeratosis (pink) alternating with parakeratosis (blue)
- Abnormal keratinocytes, especially in the lower third of the epidermis and the basal layer
- Pseudopod-like proliferations of the epidermis
- In some cases, acantholysis (acantholytic variant) is present in the lower part of the epidermis
- The dysplastic epithelium usually expands downward into the epithelium of the hair follicles
- In the upper dermis, there are solar elastosis and a sparse inflammatory infiltrate and telangiectases

Variant: Acantholytic Solar Keratosis



Hi: Suprabasal acantholysis and split formation.

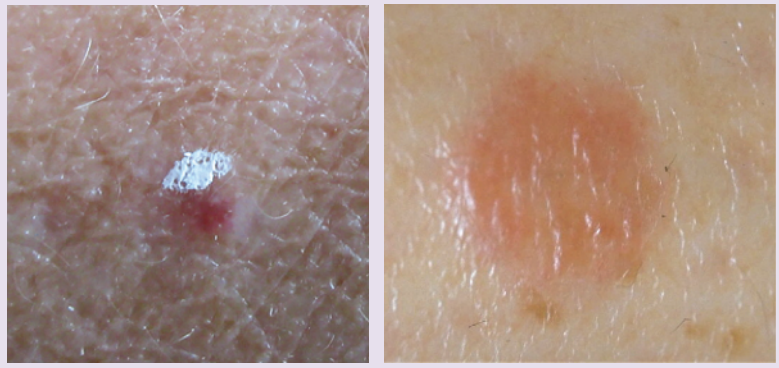
Variant: Atrophic Solar Keratosis



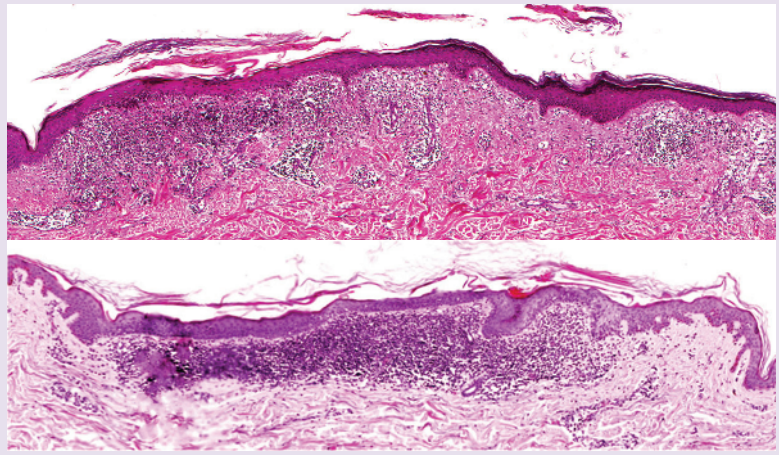
Hi: Atrophy of the epidermis.

Variant: Lichen Planus-Like Solar Keratosis

Lichen planus-like keratoses on the lower arm



Epidermal atrophy. Lichenoid infiltrate in the upper dermis

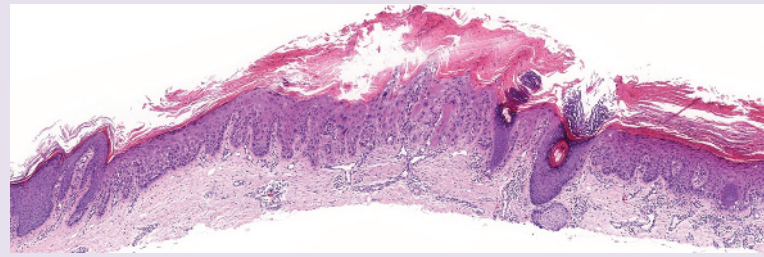


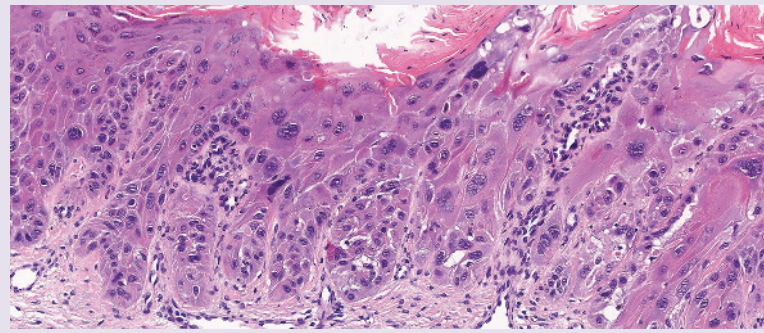
Cl: Circumscribed erythematous plaque, not necessarily hyperkeratotic.

Hi:
- Alternating para- and orthohyperkeratosis
- Acanthosis
- Lichenoid infiltrate in the upper dermis

Variant: Hypertrophic (Bowenoid) Solar Keratosis

Hyperkeratosis, acanthosis, papillomatosis, atypical keratinocytes in all levels of the epidermis featuring a bowenoid pattern





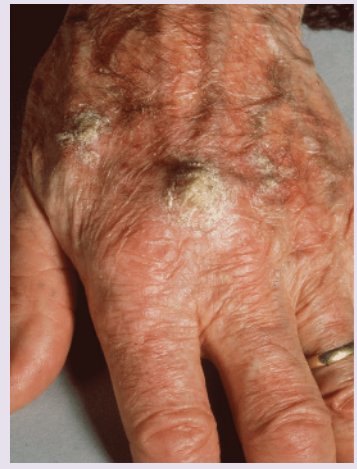
Hi:

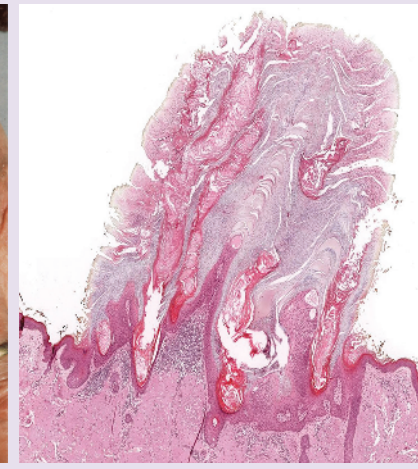
- Hypertrophic epidermis
- Bowenoid features with atypical cells in mid and lower levels of the epidermis

Cornu Cutaneum

Keratotic horn on actinic keratoses (left)

Spike-like apposition of horny masses on top of a hypertrophic actinic keratosis (right)





This clinical term describes the apposition of horny material forming a horn. It may be seen in association with various underlying disorders, including actinic keratosis, lupus erythematosus, radiation-induced scars, keratoacanthoma, squamous cell carcinoma, and several other conditions.

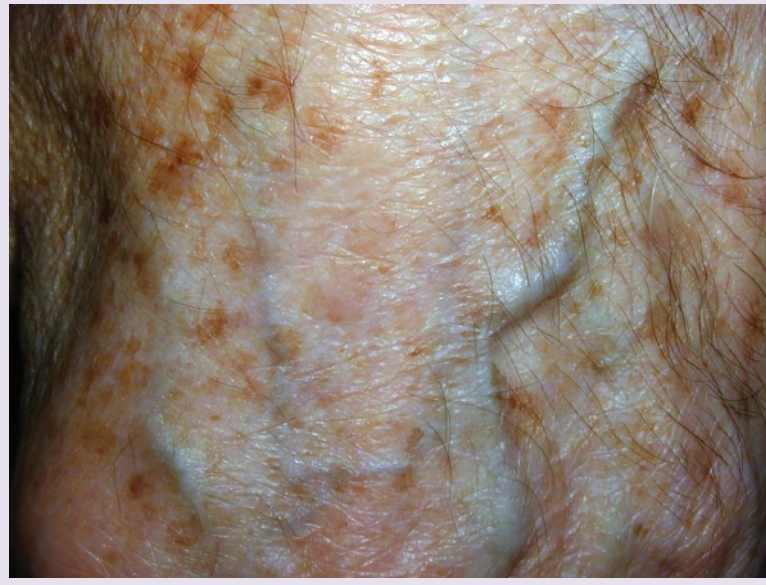
Cl: Horn-like hyperkeratosis.

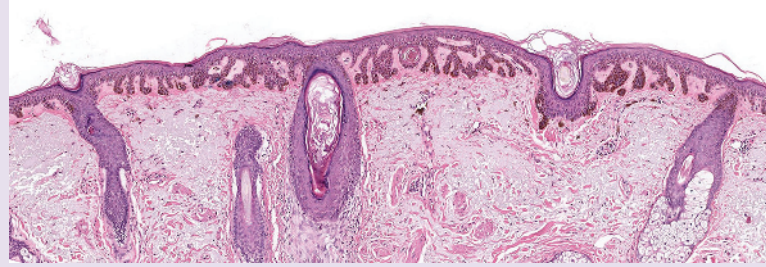
Hi:

- Massive apposition of ortho- or parakeratotic horny masses
- Specific changes of the respective underlying disorder

Acanthomas, Non-Viral

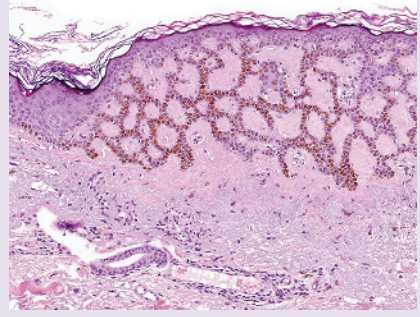
Solar Lentigo

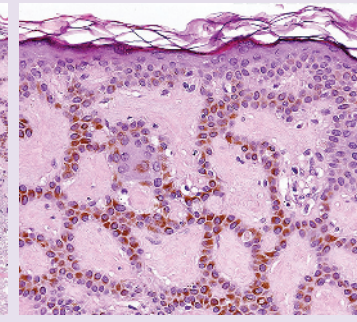




Small bud-like acanthotic proliferations of the epidermis

Actinic elastosis in the dermis



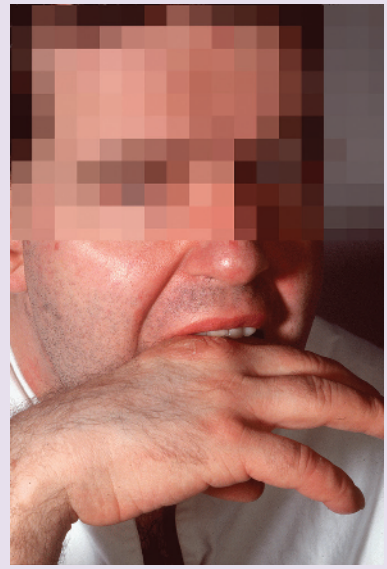


Markedly interconected hyperpigmented epidermal strands ("dirty feet")

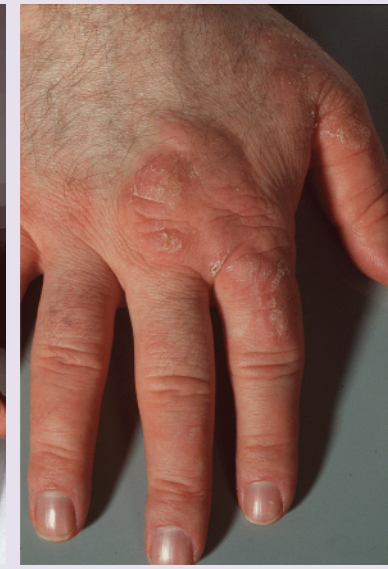
Cl: Multiple brown pigmented macules in sun-exposed locations in elderly individuals.
Hi:
- Small, bud-like acanthotic proliferations
- Anastomosing network in some cases
- Hyperpigmentation of the basal layer
- Variable increase of melanocytes
- Solar elastosis in the upper dermis

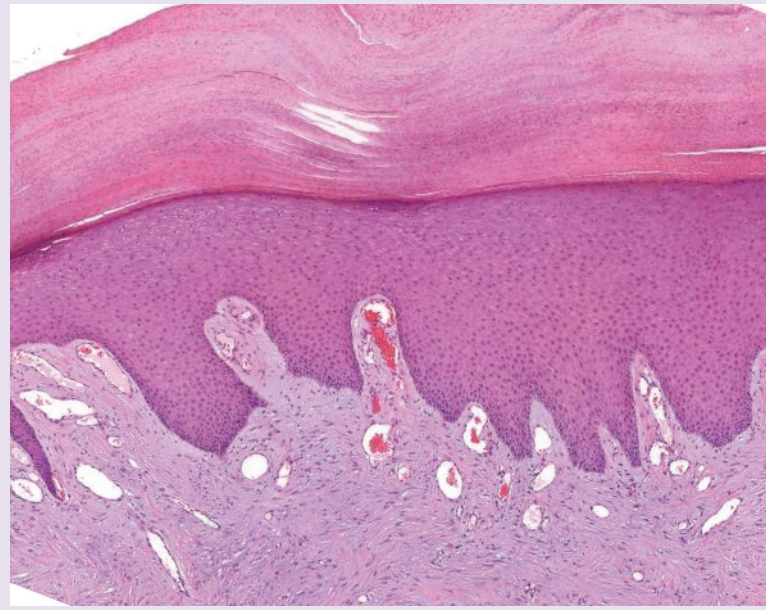
DD: Pigmented actinic (solar) keratosis and flat seborrheic keratosis.

Callus, Factitial Acanthoma



Factitial acantoma from chewing





Alternating stratified ortho- and parakeratosis

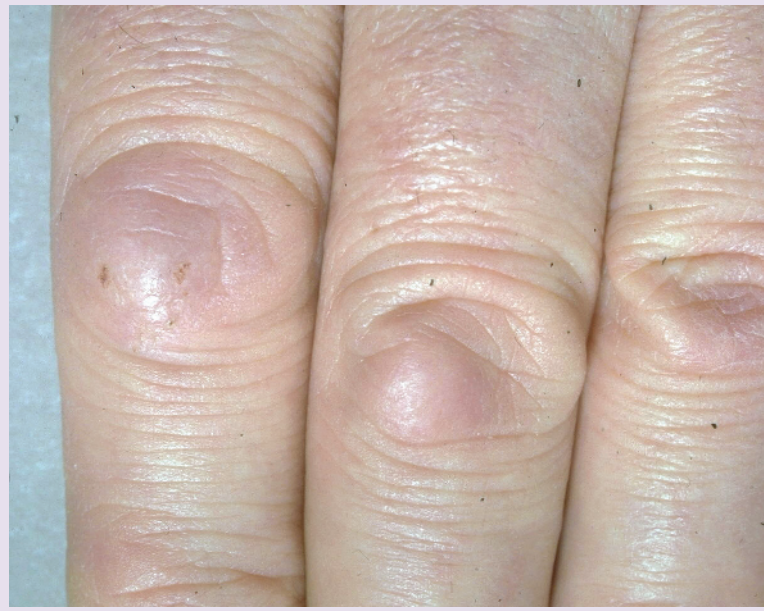
Marked acanthosis with plump rete ridges

Cl: Corns typically develop in response to pressure and show compact apposition of horny material, sometimes surrounded by faint erythema.

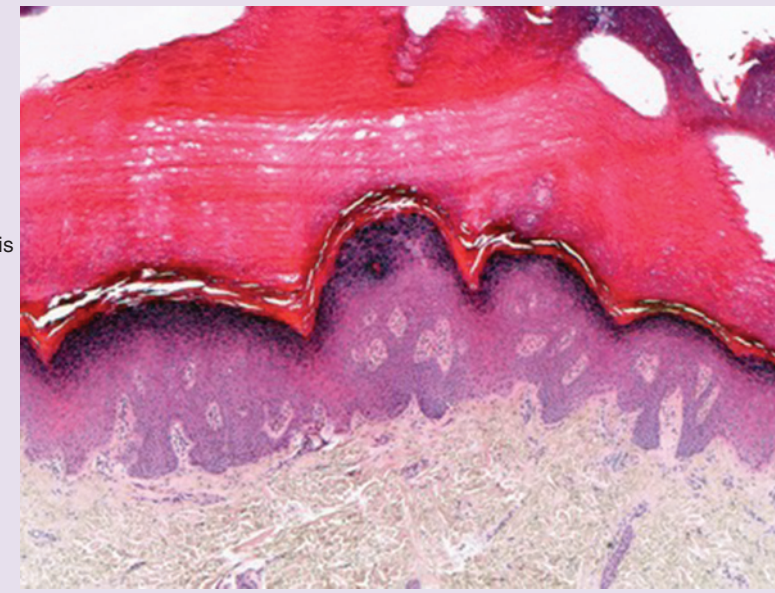
Hi:

- Alternating stratified ortho- and parahyperkeratosis
- Acanthosis of the epidermis without koilocytes
- Pseudopod-like rete ridges
- Granular layer normal or prominent
- Fibrosis and telangiectases

Knuckle Pads (Chewing Pads)



Knuckle pads in typical location

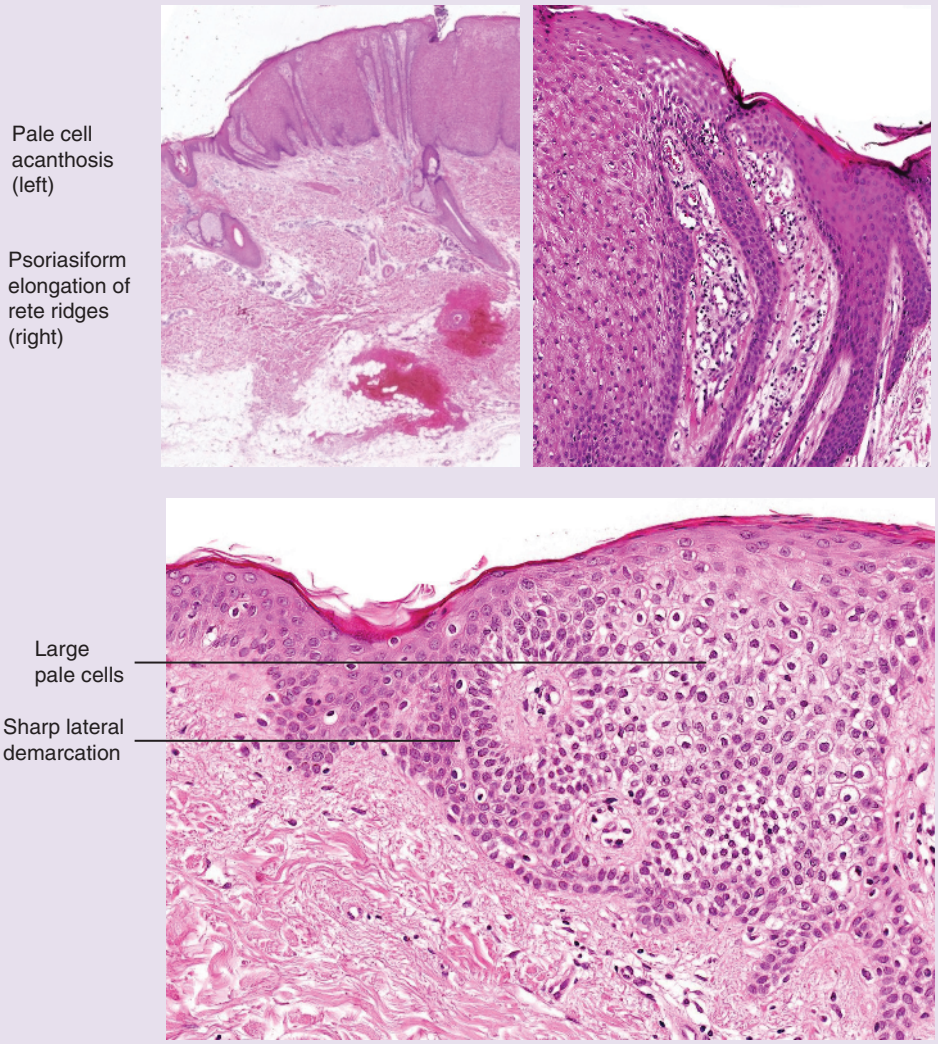


Hyperorthokeratosis with hypergranulosis and marked acanthosis

Cl: Knuckle pads, usually located at the dorsal aspect of the joints of the finger, are considered a subtype of callus.

Hi: See above (callus).

Pale (Clear) Cell Acanthoma



Cl: This uncommon, benign, slowly exophytic growing and slightly hyperkeratotic tumor usually presents as a solitary sharply bordered lesion on the leg of elderly individuals.

Hi:

- Slight hyperkeratosis
- Acanthotic epidermis, dominated by large pale cells which replace all but the basal layer
- Sharp demarcation against the adjacent normal epidermis
- Large cells are rich in glycogen (PAS)
- Psoriasiform elongation of rete ridges

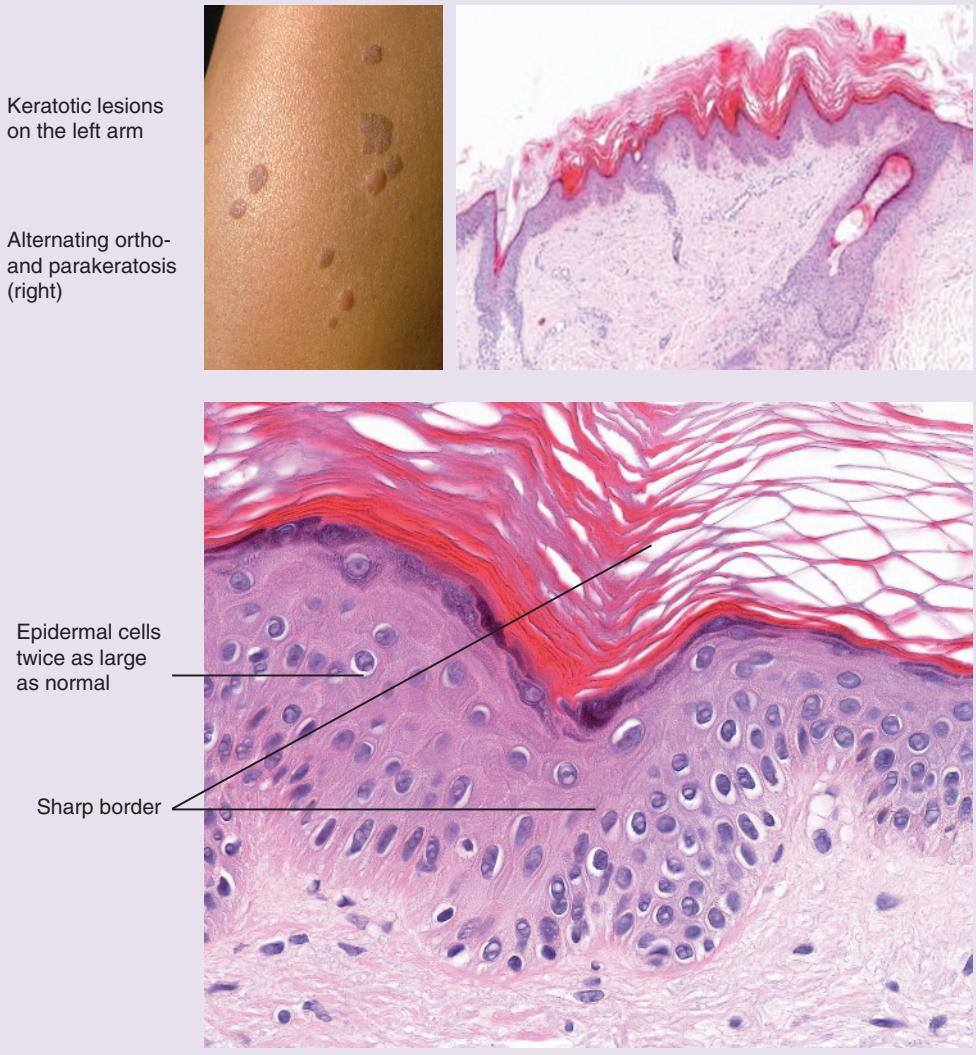
References

Garcia-Gavin, J., Gonzalez-Vilas, D., Montero, I., Rodriguez-Pazos, L., Pereiro, M.M., and Toribio, J. (2011) Disseminated eruptive clear cell acanthoma with spontaneous regression: further evidence of an inflammatory origin? *Am J Dermatopathol* **33**(6): 599–602.

Lin, C.Y., Lee, L.Y., and Kuo, T.T. (2016) Malignant clear cell acanthoma: report of a rare case of clear cell acanthoma-like tumor with malignant features. *Am J Dermatopathol* **38**(7): 553–6.

Shalin, S.C., Rinaldi, C., and Horn, T.D. (2013) Clear cell acanthoma with changes of eccrine syringofibroadenoma: reactive change or clue to etiology? *J Cutan Pathol* **40**(12): 1021–6.

Large Cell Acanthoma



Cl: This pale flat benign tumor with sharp borders in sun-exposed areas is considered to be a variant of solar keratosis and is a histological rather than a clinical diagnosis.

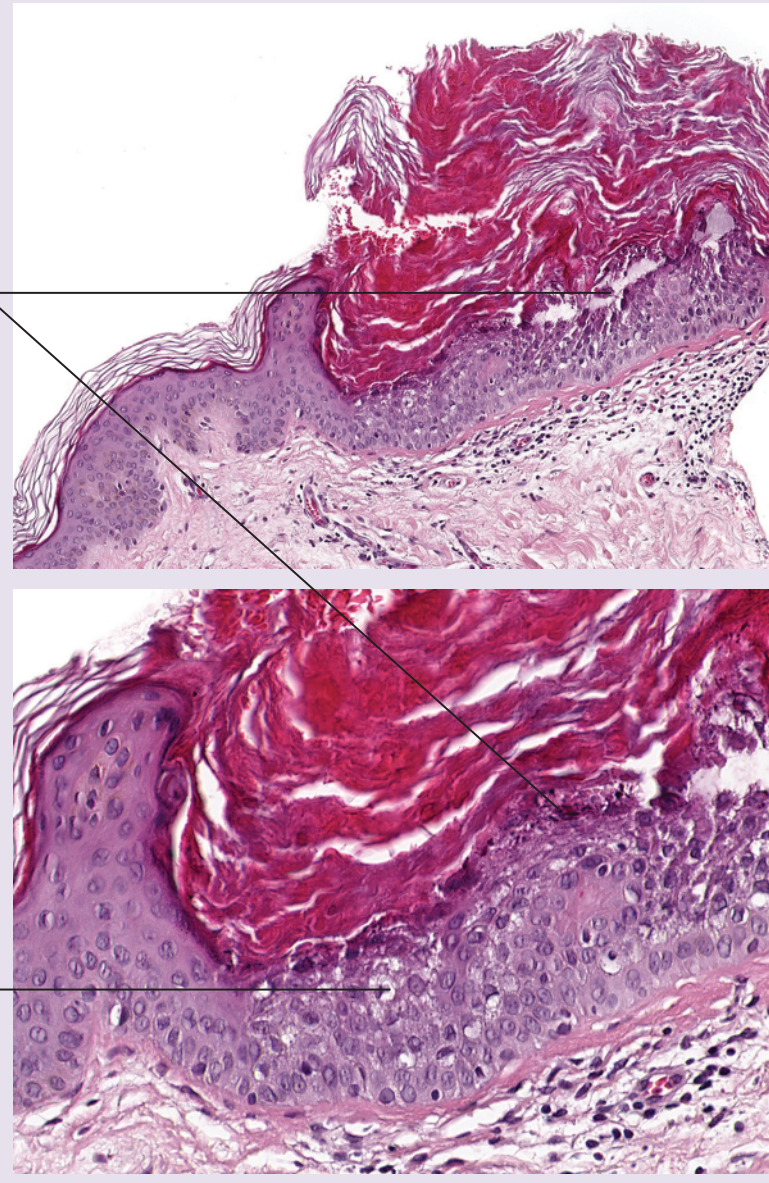
Hi:

- Hyperkeratosis
- Keratinocytes are twice as large as in normal epidermis
- Sharp demarcation from adjacent normal epidermis

Reference

Fraga, G.R., and Amin, S.M. (2014) Large cell acanthoma: a variant of solar lentigo with cellular hypertrophy. *J Cutan Pathol* **41**(9): 733–739.

Differential Diagnosis: Epidermolytic Acanthoma



Cl: Epidermolytic acanthoma are uncommon solitary or disseminated benign tumors on the trunk or in the anogenital region presenting as wart-like lesions.

Hi:

- Hyper- and dyskeratosis
- Vacuolisation in the spinous and granular layer
- Keratohyaline granules
- Suprabasal epidermolytic cells in the upper two-thirds of the epidermis
- Suprabasilar vesiculation may occur

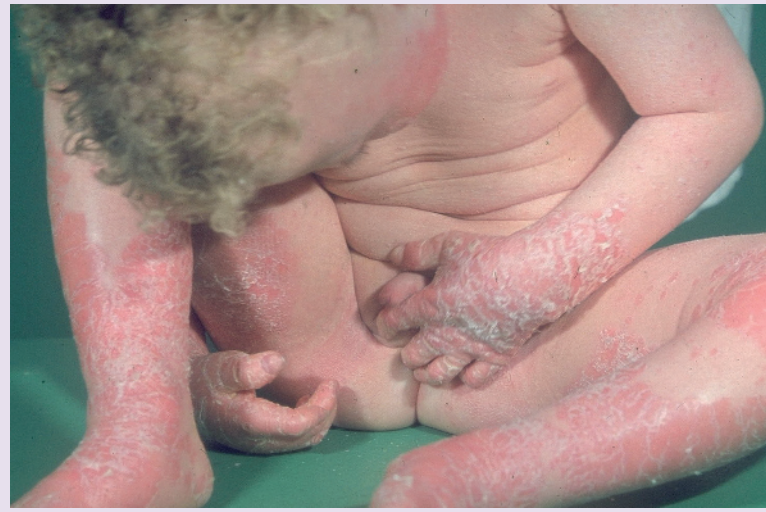
DD: Epidermolytic hyperkeratosis as seen in congenital ichthyosiform erythroderma, incidental finding in other lesions such as actinic keratosis, transient acantholytic dermatosis (Grover's), dyskeratosis follicularis (Darier's).

References

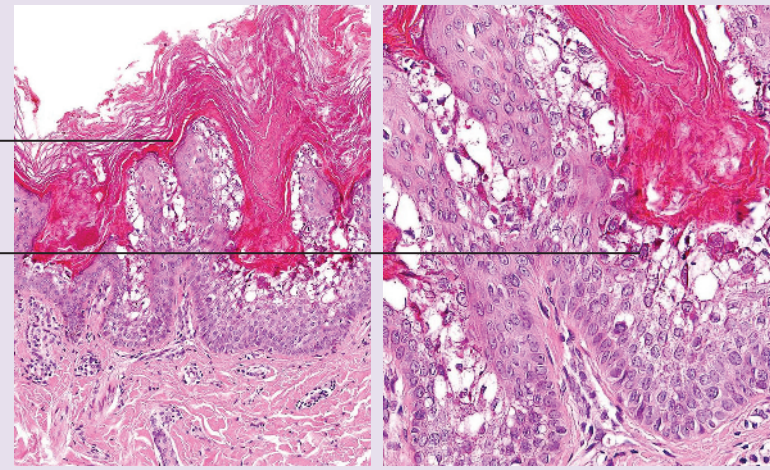
Egozi-Reinman, E., Avitan-Hersh, E., Barzilai, A., Indelman, M., and Bergman, R. (2016) Epidermolytic acanthoma of the genitalia does not show mutations in KRT1 or KRT10. *Am J Dermatopathol* **38**(2): 164–5.

Kazlouskaya, V., Lambe, J., and Elston, D. (2013) Solitary epidermolytic acanthoma. *J Cutan Pathol* **40**(8): 701–707.

Differential Diagnosis: Congenital Ichthyosiform Erythroderma



Eczema-like skin lesions in a child



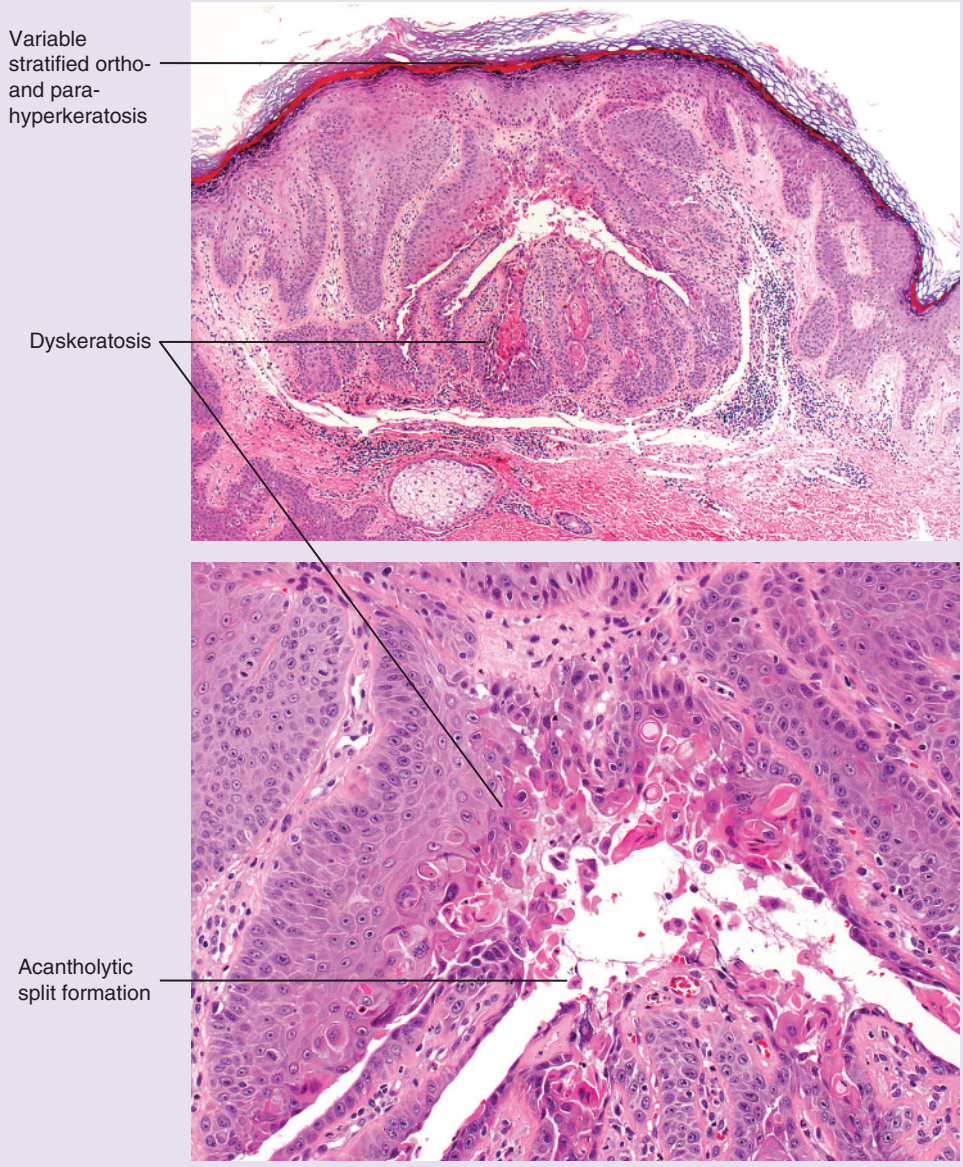
Inborn keratinization disorder with widespread skin lesions at birth or early in life.

Cl: Widespread erythroderma with blistering transforming to warty plaques, preferentially located in big flexural skinfolds.

Hi:

- Thick epidermis
- Acanthokeratolysis
- Clumps of keratin tonofilaments

Acantholytic Acanthoma



Cl: Solitary or multiple papules most commonly found on the trunk, anogenital or mucosal areas, resembling verruca vulgaris or seborrheic keratosis. Immunosuppression may be an underlying pathogenetic factor.

Hi:

- Variable hyperkeratosis
- Symmetrical, well-circumscribed downward proliferation of keratinocytes without atypia
- Dyskeratosis
- Prominent acantholysis throughout all epidermal layers is the hallmark of the lesions

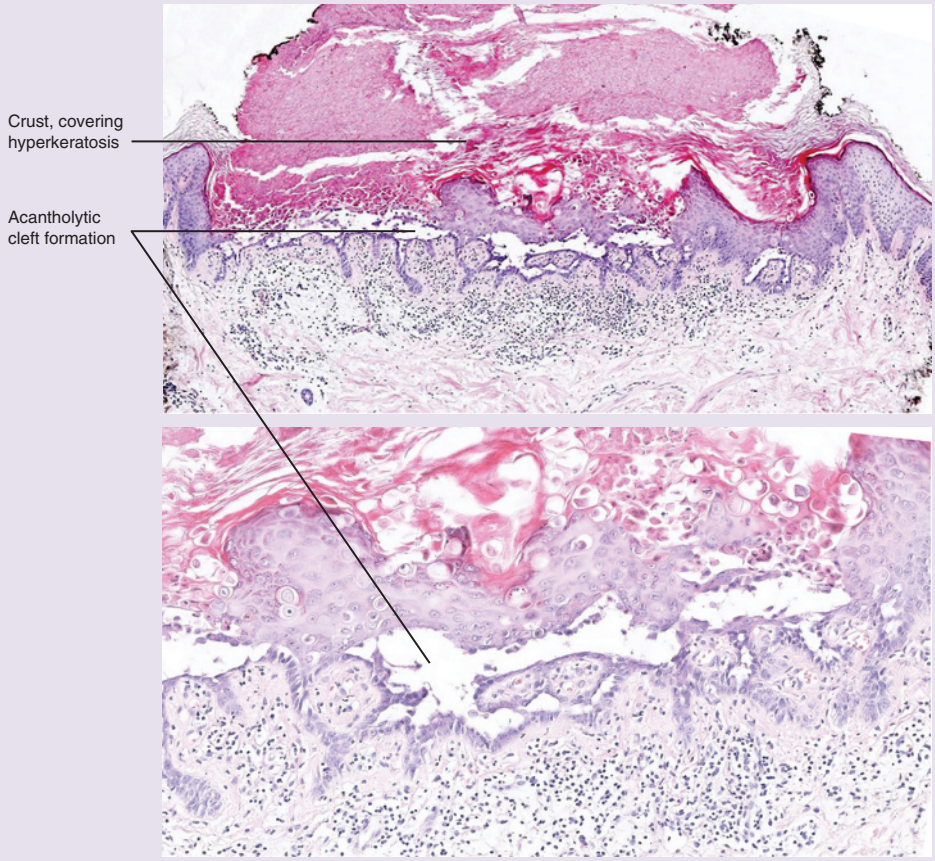
DD: Resembles Hailey–Hailey, Grover's or pemphigus, but the process is localized.

References

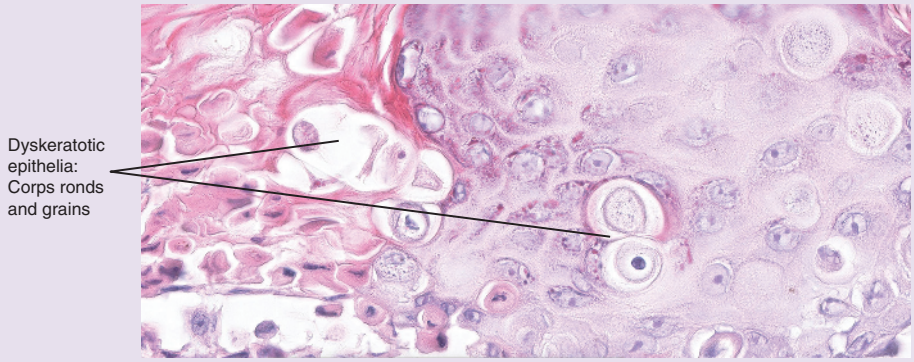
Brownstein, M.H. (1988) Acantholytic acanthoma. *J Am Acad Dermatol* **19**(1): 783–6.

Megahed, M., and Scharffetter-Kochanek, K. (1993) Acantholytic acanthoma. *Am J Dermatopathol* **15**(3): 283–5.

Warty Dyskeratoma



Warty Dyskeratoma



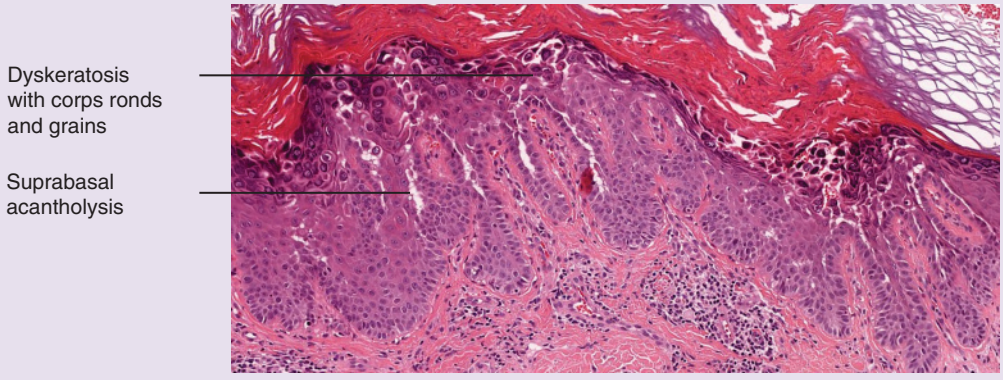
Cl: Solitary verrucous papule, sometimes crusted when traumatized.

Hi: Warty dyskeratoma simulates the histological features of Darier's disease and has been considered to be a localized variant of that disease.

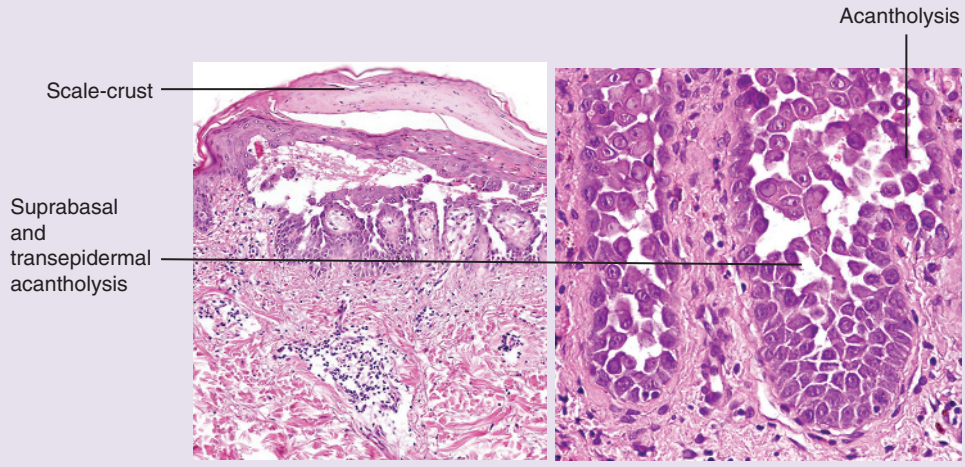
- Papular or verrucous lesion
- Focal parakeratosis
- Irregular acanthosis with acantholysis
- Dyskeratotic corps ronds and grains
- Frequent association with pilosebaceous structures

DD: Dyskeratosis follicularis (Darier's disease; see Volume I, page 65), pemphigus benignus familiaris (Hailey–Hailey; see Volume I, page 64), transient acantholytic dermatosis (Grover's disease; see Volume I, page 67).

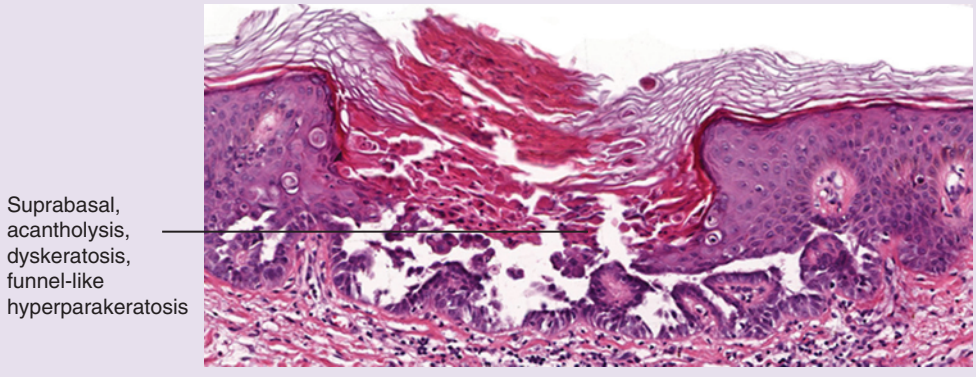
DD: Dyskeratosis Follicularis (Darier)



DD: Pemphigus Benignus Familiaris (Hailey-Hailey)



DD: Transient Acantholytic Dermatosis (Grover's Disease)



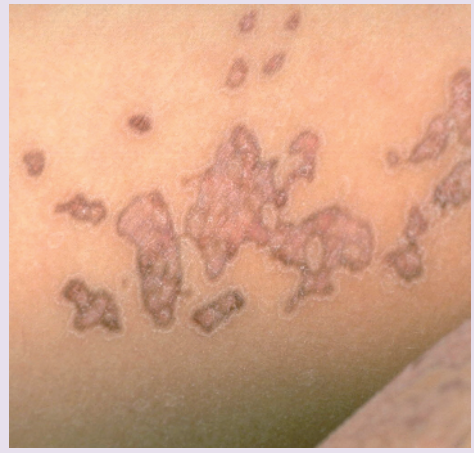
References

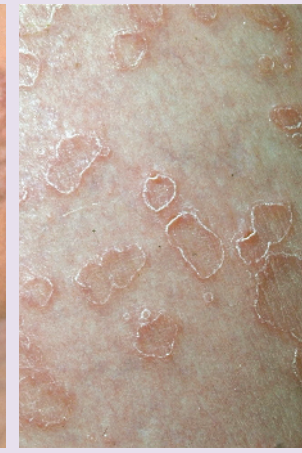
Lora, V., Scarabello, A., and Cota, C. (2015) Warty dyskeratoma as a cutaneous horn of the mons pubis. *Am J Dermatopathol* **37**(10): 802–4.

Martorell-Calatayud, A., Sanmartin-Jimenez, O., Traves, V., and Guillen, C. (2012) Numerous umbilicated papules on the trunk: multiple warty dyskeratoma. *Am J Dermatopathol* **34**(6): 674–5.

Porokeratoma (Porokeratosis Mibelli)

Slightly atrophic patches with hyperkeratotic borders

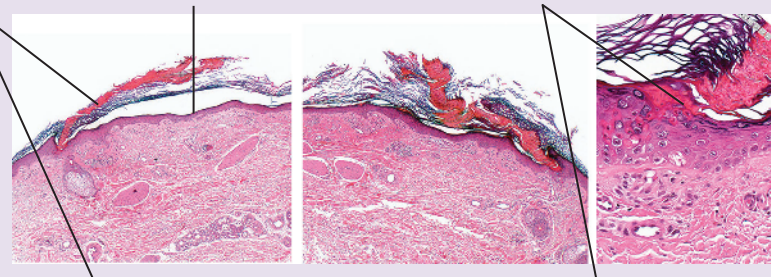


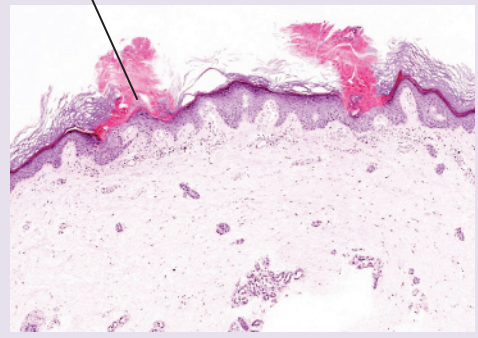


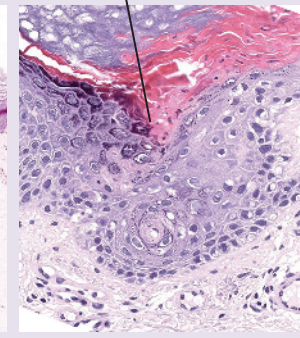
Cornoid lamellae on opposite sides

Atrophy of the epidermis

Para- and dyskeratosis







This group of autosomal dominant inherited keratinization disorders is defined histologically by the presence of a cornoid lamella, which is seen best when the biopsy is taken perpendicular to the border of the lesion.

Cl: The lesions may appear at any age and occur more often in men. The extremities are the favored sites of manifestation, but other parts of the body may also be affected. The initial lesion starts as a small red papule with a central keratotic spine which spreads peripherally, forming a slightly atrophic patch with irregular hyperkeratotic borders. Linear porokeratosis and giant porokeratosis are variants. There is an increased risk for the development of squamous cell carcinoma.

Hi:

- No relationship to sweat pores, as suggested by the name
- Narrow ridge of hyperkeratosis with parakeratosis (cornoid lamella)
- Cornoid lamella (with PAS-positive grains) amidst parakeratotically layered corneocytes
- Dyskeratotic cells are almost always found beneath the cornoid lamella
- Focal absence of stratum granulosum
- Central atrophy of the epidermis – imitating atrophic lupus erythematosus
- Underlying lichenoid infiltrate
- Advanced stages may show epithelial dysplasia in the center

References

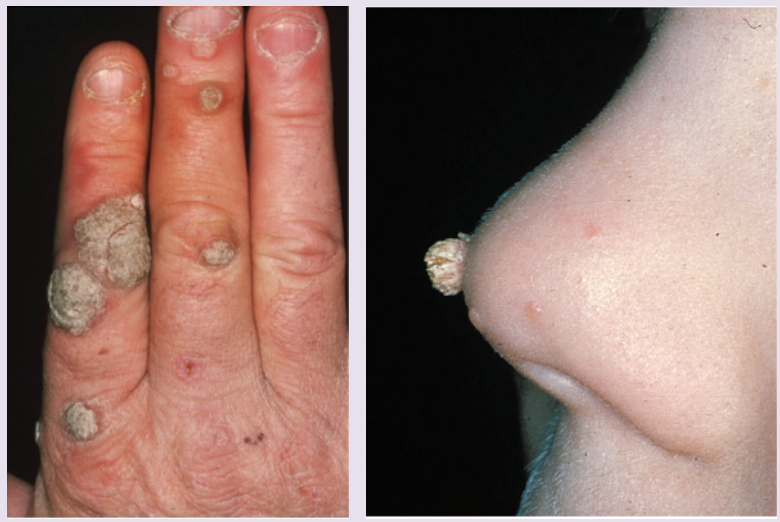
Biswas, A. (2015) Cornoid lamellation revisited: apropos of porokeratosis with emphasis on unusual clinicopathological variants. *Am J Dermatopathol* **37**(2): 145–55.

Tallon, B., and Emanuel, P. (2017) Follicular porokeratosis, a porokeratosis variant. *Am J Dermatopathol* **39**: e1-7–e109.

Tan, T.S., and Tallon, B. (2016) Pigmented porokeratosis. A further variant? *Am J Dermatopathol* **38**(3): 218–21.

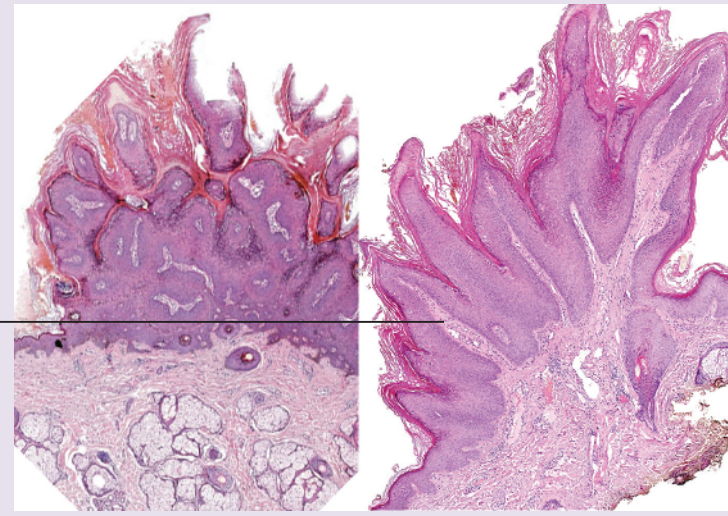
Acanthomas, Viral

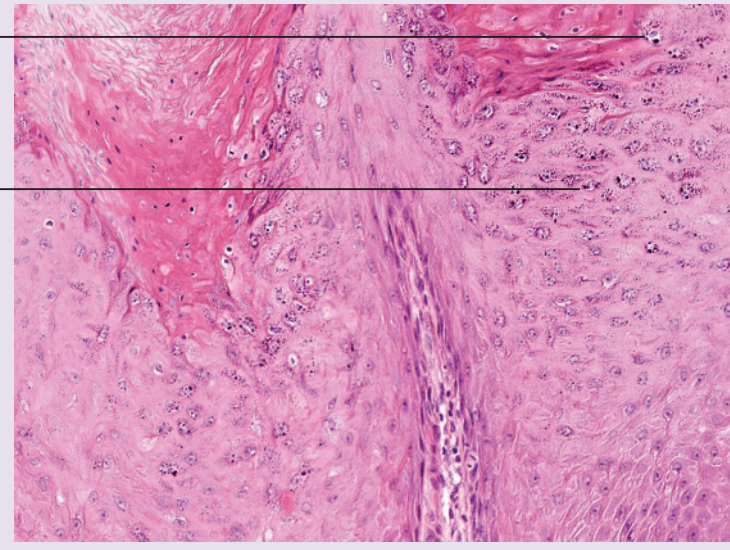
Verruca Vulgaris

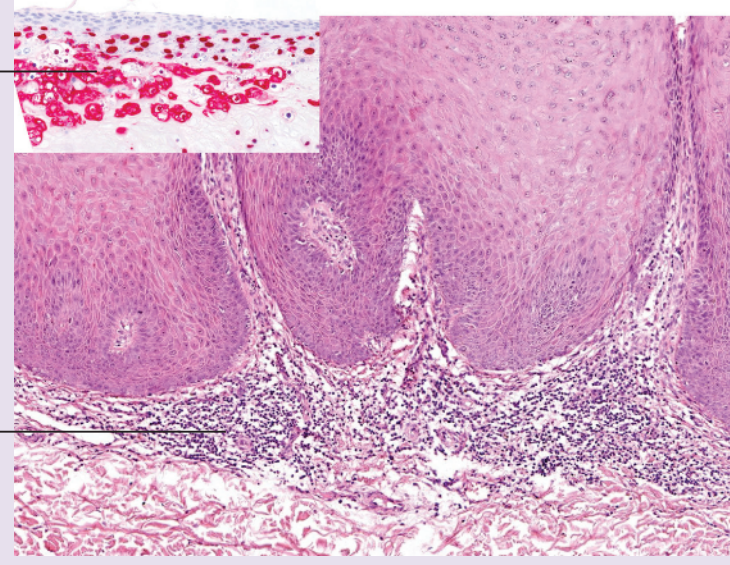


Hyperkeratotic verrucae on fingers and nose

Verruca Vulgaris







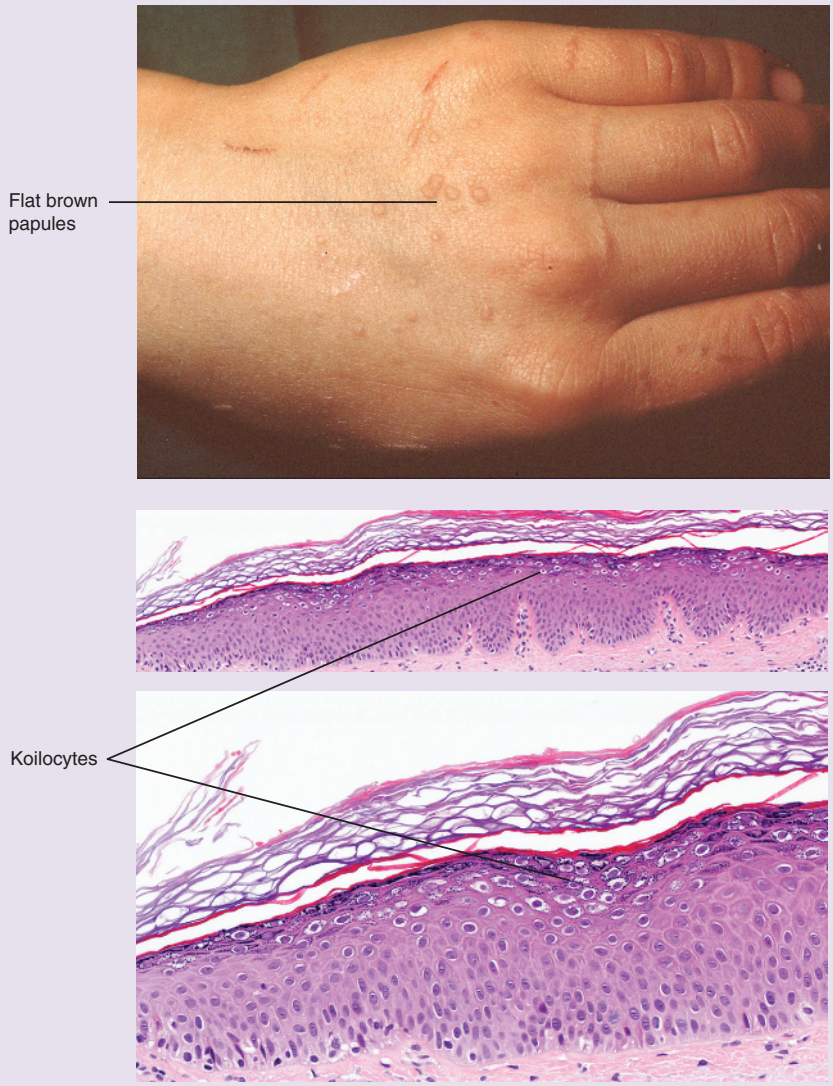
HUMAN PAPILLOMA VIRUS (HPV)

Cl: Solitary or grouped papules showing massive hyperkeratosis and sometimes significant inflammation.

Hi:

- Epidermal hyperplasia with a "multiple raised fingers" silhouette
- Hyperkeratosis with focal parakeratosis
- Intracorneal inclusions of hemorrhagic exudate (capillary thrombi)
- Hypergranulosis with enlarged keratohyalin granules
- Koilocytes (bird's eye cells) in the granular layer and upper stratum spinosum
- Dilated vessels in the papillary dermis
- Inflammatory infiltrate in the upper dermis

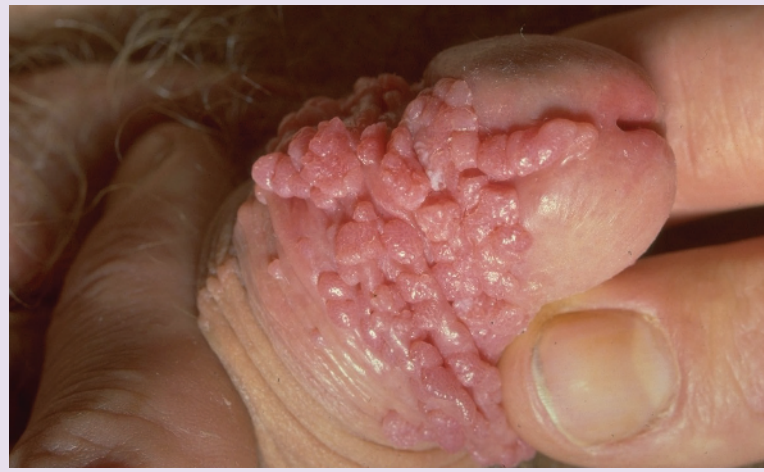
Variant: Verruca Plana

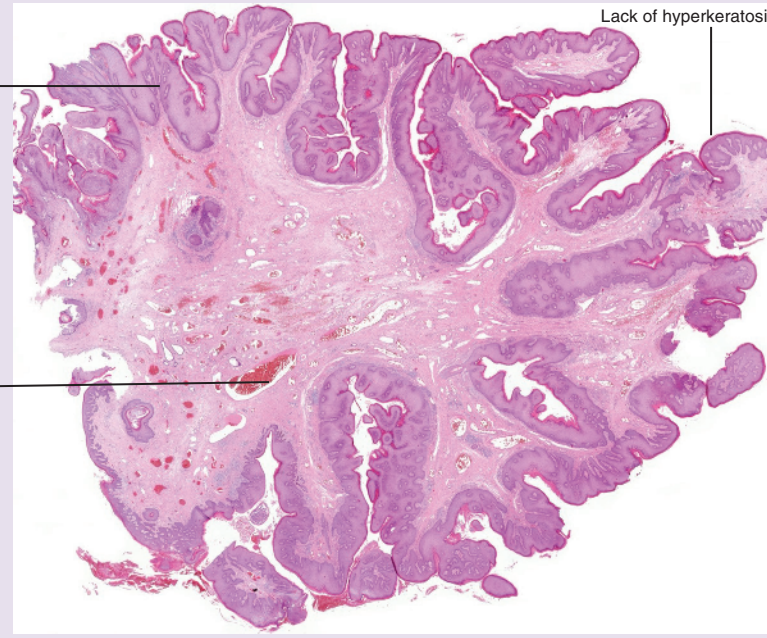


HUMAN PAPILLOMA VIRUS (HPV)

Cl: Flat hyperkeratotic (verruciform) papules.
Hi:
- Hyperkeratosis
- Slight acanthosis
- No papillomatosis
- Confluent band of koilocytes (bird's eye cells) in the granular layer

Variant: Condyloma Acuminatum



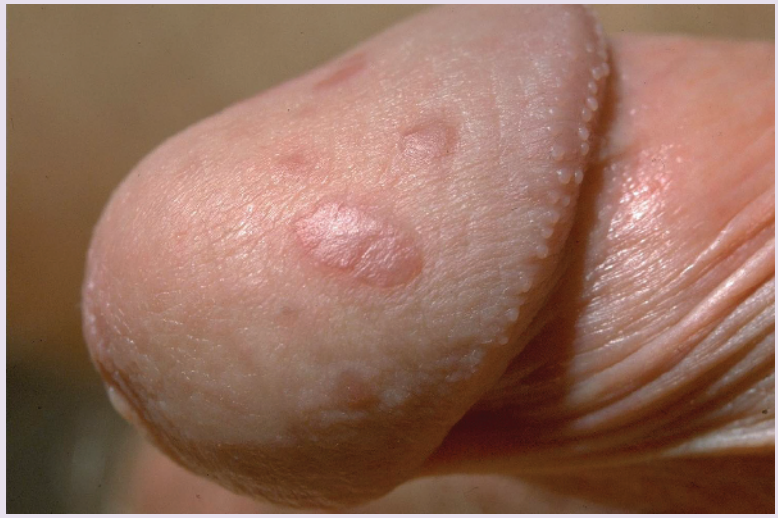


Cl: Papular and verruciform lesions in anogenital or oral localisation.
Hi: Acanthopapilloma with focal hyperparakeratosis and lack of pseudocysts ("naked seborrheic keratosis"). Presence of koilocytes, even sometimes sparse.

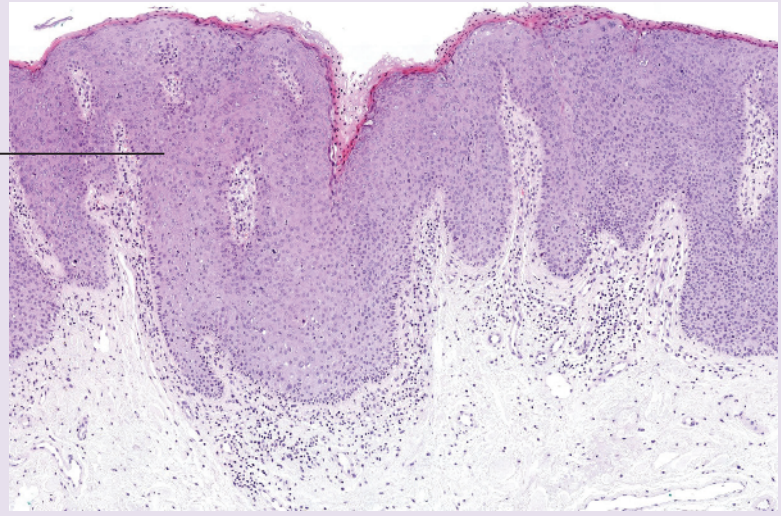
HUMAN PAPILLOMA VIRUS (HPV)

Bowenoid Papulosis

Flat papules

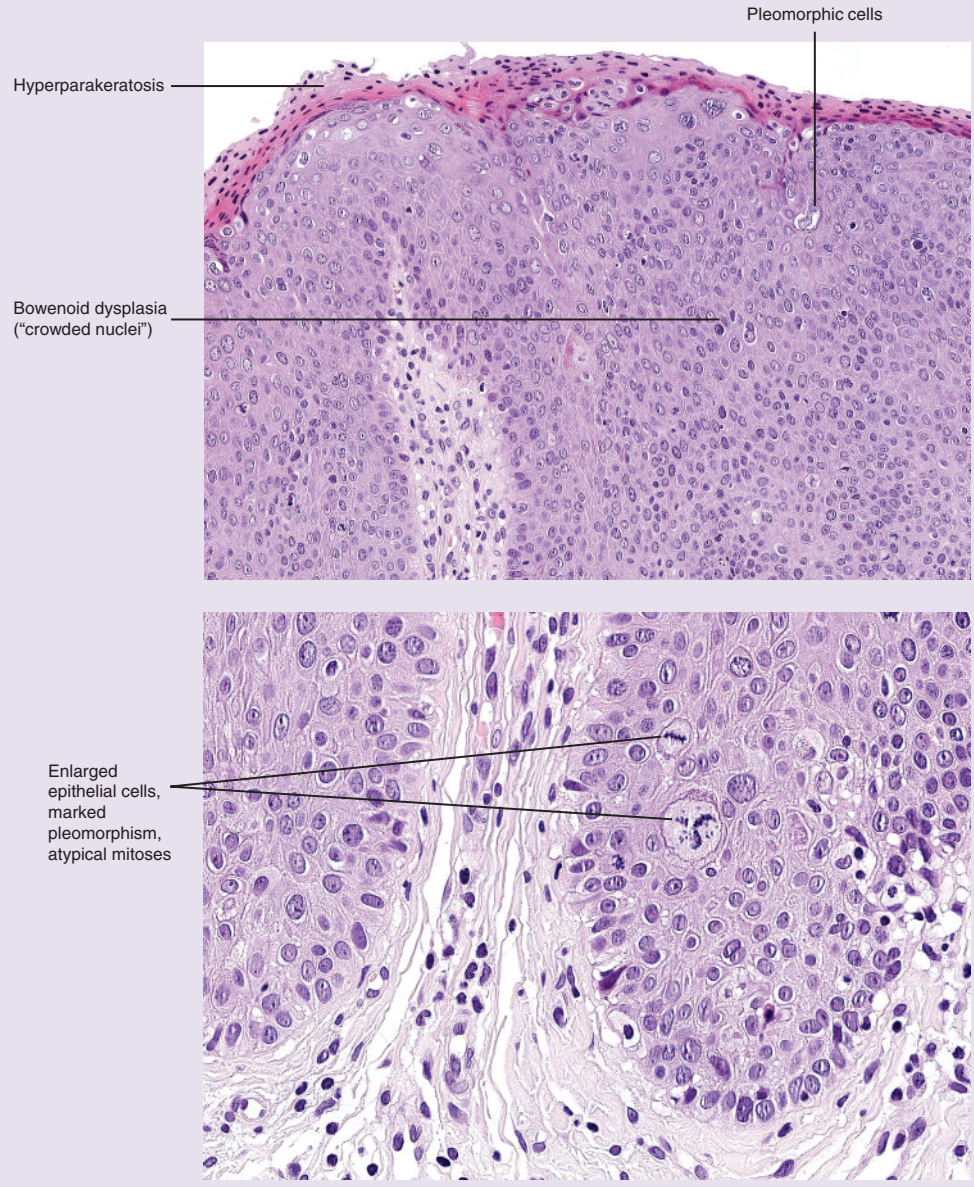


Acanthosis, papillomatosis, marked dysplasia



HUMAN PAPILLOMA VIRUS (HPV)

Bowenoid Papulosis



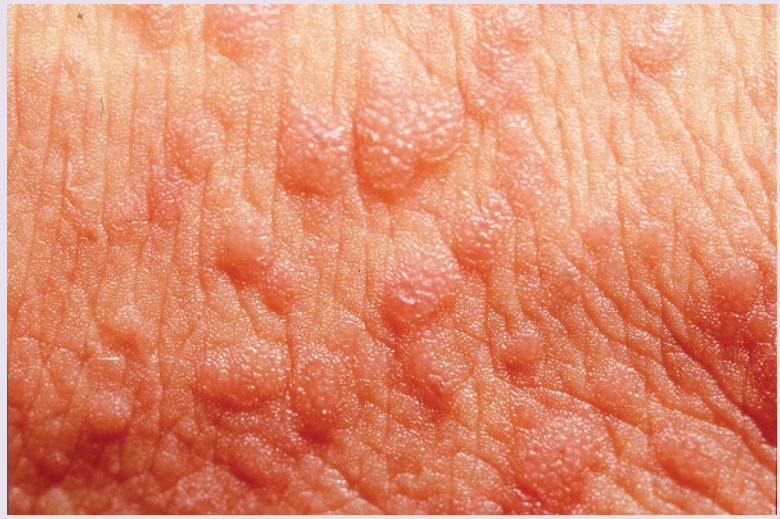
Cl: Solitary or confluent flat papular eruptions in anogenital localisation, often associated with oncogenic HPV infection (HPV16, HPV18).

Hi: Atypical epithelial cells with nuclear pleomorphism and mitotic activity, identical with Bowen's disease.

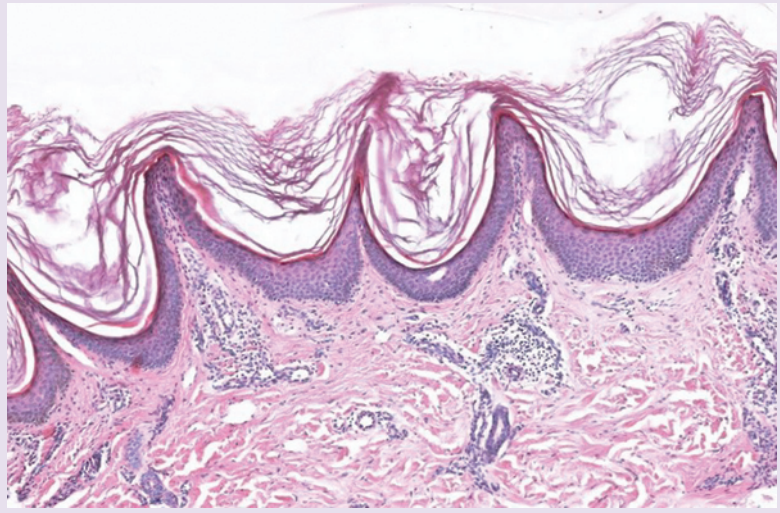
HUMAN PAPILLOMA VIRUS (HPV)

Acrokeratosis Verruciformis (Hopf)

Flat hyperkeratotic papules on the dorsum of the hand



Hyperkeratosis, wavy acanthosis, papillomatosis



Considered to be associated with HIV infection by some and to be an autosomal dominant inherited disorder by others. There is close relationship to Darier's disease and to epidermodysplasia verruciformis.

Cl: Multiple flat hyperkeratotic papules in distal parts of the extremities (dorsa of the hands, feet, forearms).

Hi:

- Orthohyperkeratosis
- Wavy acanthosis
- Papillomatosis
- Thin papillae

MOLLUSCUM POXVIRUS

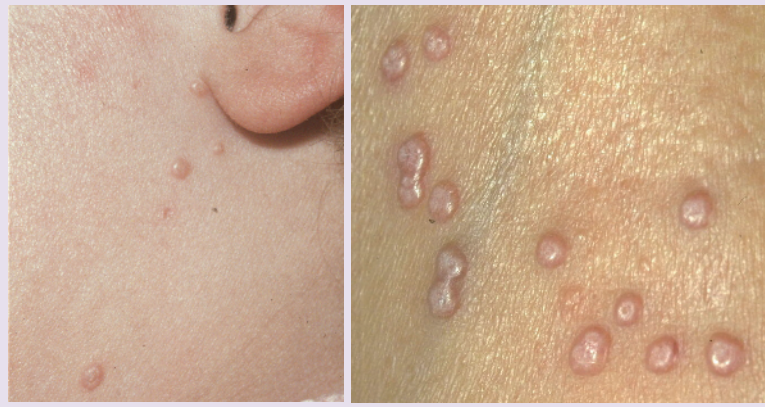
References

Bergman, R., Sezin, T., Indelman, M., Helou, W.A., and Avitan-Hersh, E. (2012) Acrokeratosis verruciformis of Hopf showing P602L mutation in ATP2A2 and overlapping histopathological features with Darier disease. *Am J Dermatopathol* **34**(6): 597–601.

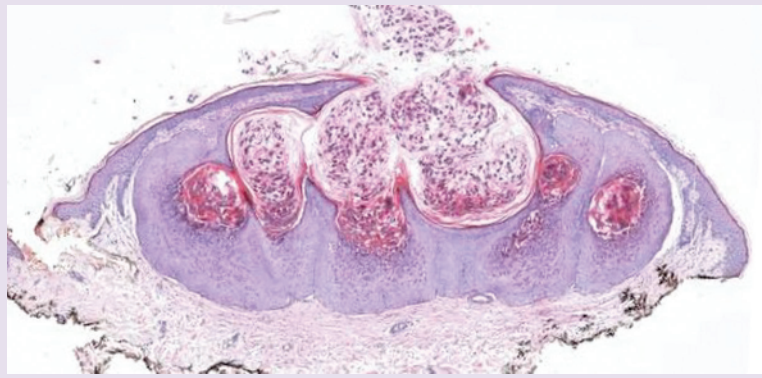
Matsumoto, A., Gregory, N., Rady, P.L., Tyring, S.K., and Carlson, J.A. (2017) Brief Report: HPV-17 infection in Darier disease with acrokeratosis verrucosis of Hopf. *Am J Dermatopathol* **39**(5): 370–3.

Molluscum Contagiosum

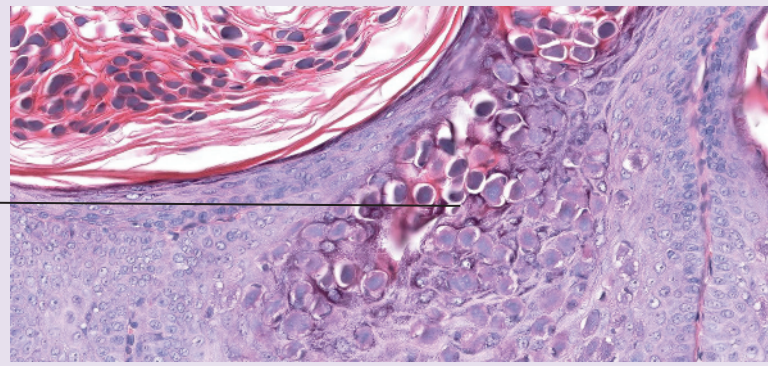
Grouped umbilicated papules



Crateriform symmetric tumor with Molluscum bodies



Molluscum bodies (basophilic virus capsid – Molluscum poxvirus)



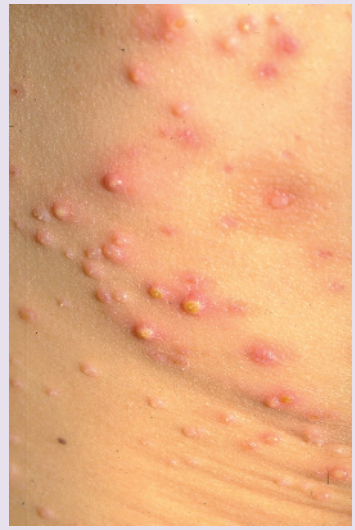
MOLLUSCUM POXVIRUS

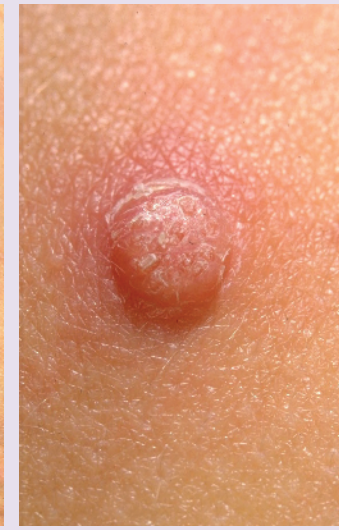
Cl: Molluscum poxvirus is the causative agent. Typically children and immunocompromised patients are affected. Lesions are mostly multiple, sometimes extensive and eczematous. Characteristic features are elevated papules with a central dell.

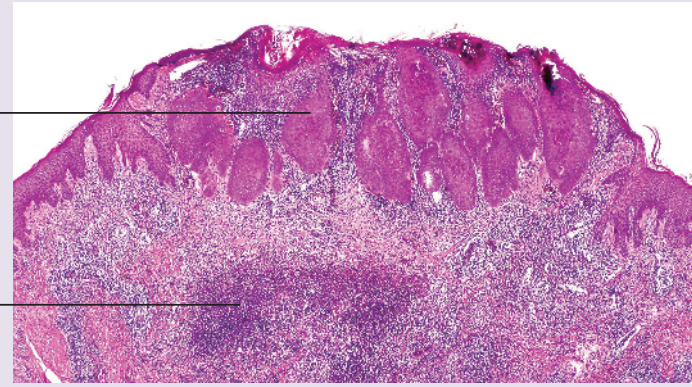
Hi:

- Epidermal hyperplasia
- Central invagination, corresponding to the clinically visible dell
- Dell filled with necrotic keratinocytes, containing large, prominent, basophilic intracytoplasmic inclusions (molluscum bodies) that stain positive with Melan A
- Massive inflammatory reaction when ruptured

Molluscum Contagiosum, Inflamed







Reference

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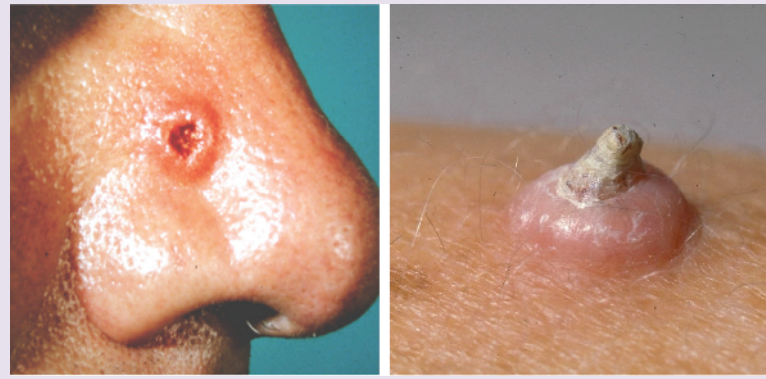
"Pseudocarcinomas" and Neoplasms with Intermediate Malignant Potential

Keratoacanthoma, epithelioma cuniculatum, papillomatosis cutis carcinoides, Buschke–Löwenstein giant condyloma, and florid oral papillomatosis form a group of disorders which are biologically benign, do not metastasize and histologically simulate large warts or well-differentiated squamous cell carcinoma.

Keratoacanthoma (KA)

Hyperkeratotic craterifom tumor on the nose (left)

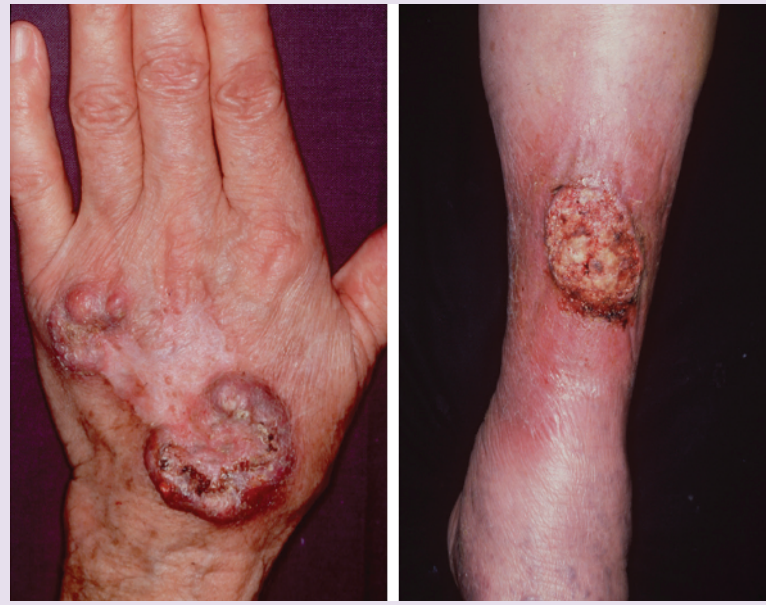
Nodule with central keratotic horn (right)



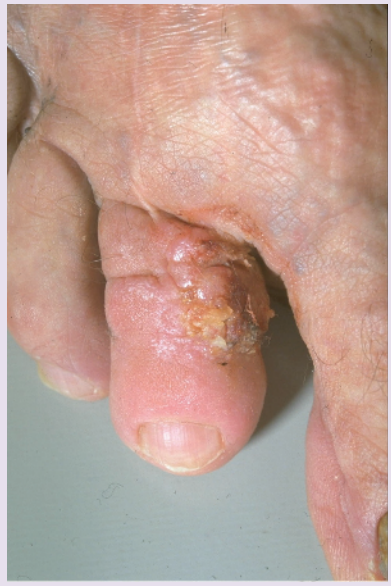
Cl: Most KAs develop in sun-exposed areas. They are biologically benign and develop within weeks, in contrast to squamous cell carcinoma which develops over months. Multiple KAs are encountered in conjunction with hereditary cancer syndromes (Muir–Torre) or as specific clinical variants (e.g. Grzybowski, Ferguson–Smith). The typical lesion is a dome-shaped keratotic nodule with a central dell filled by a keratotic plug. KA centrifugum marginatum is a centrifugal spreading variant, which most commonly occurs on the extremities.

Variant: Keratoacanthoma Centrifugum Marginatum

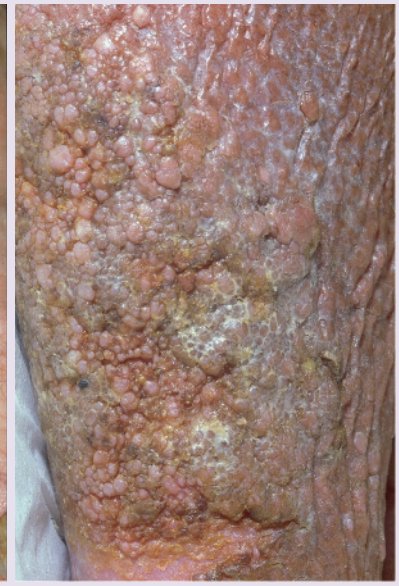
Centrifugally growing flat hyperkeratotic tumors on hand (left) and lower limb (right)



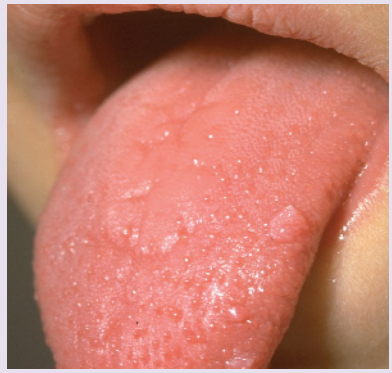
Variants of Keratoacanthoma

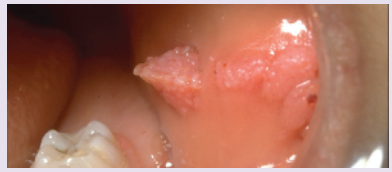


Verrucous carcinoma
(epithelioma cuniculatum)

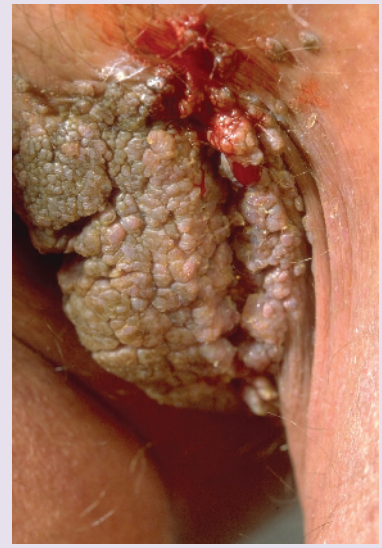


Papillomatosis cutis carcinoides
(pseudocarcinomatous hyperplasia)



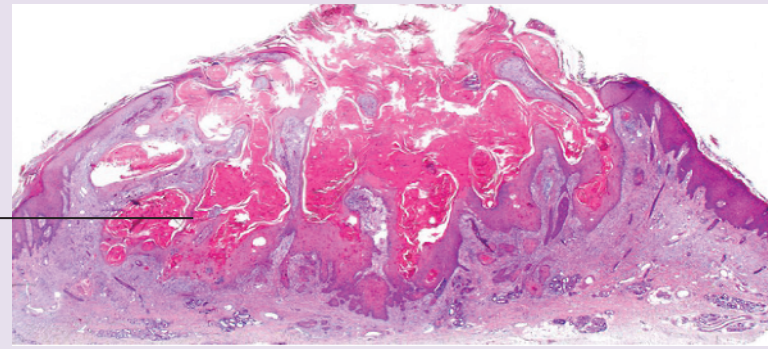


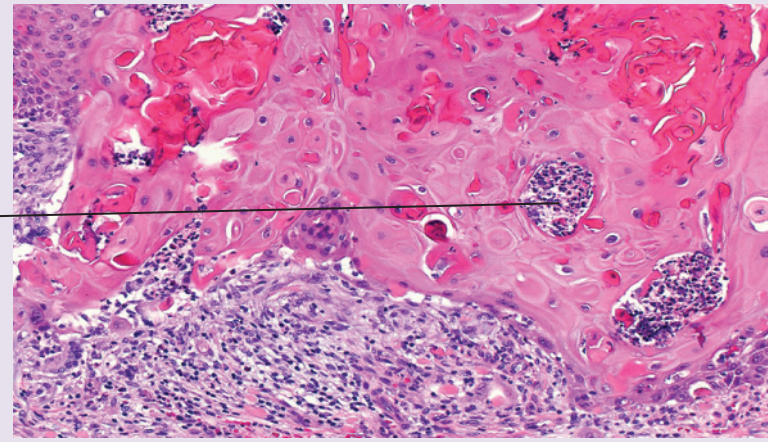
Florid oral papillomatosis

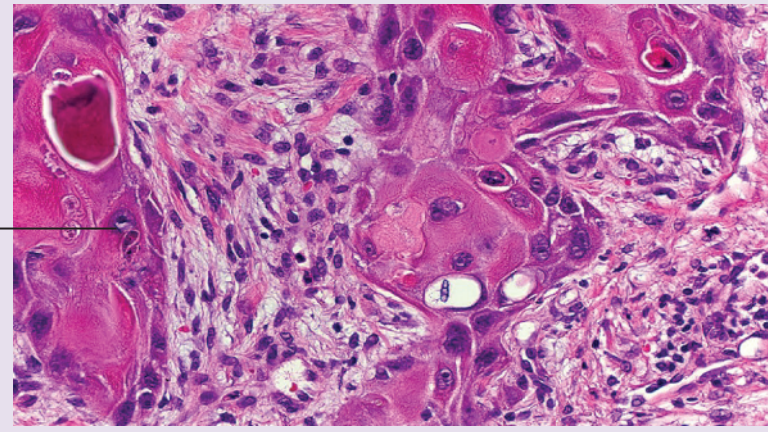


Giant condyloma
(Buschke–Löwenstein)

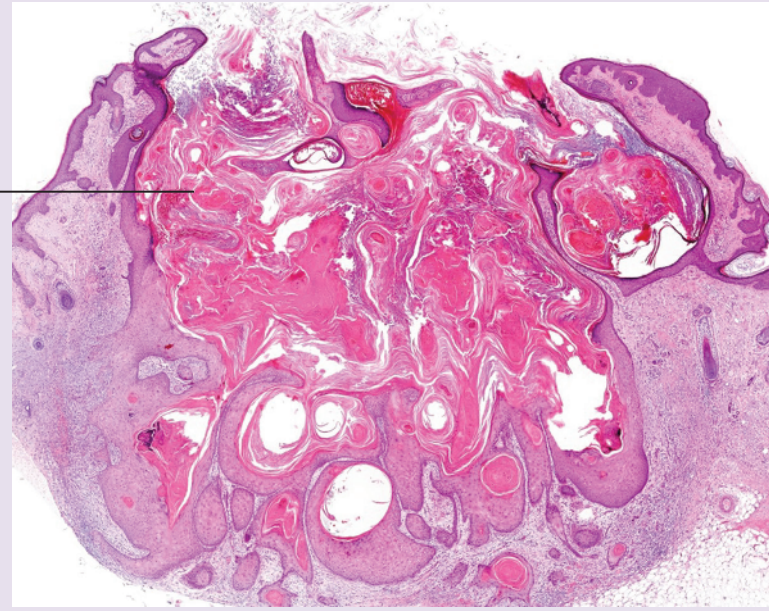
Keratoacanthoma

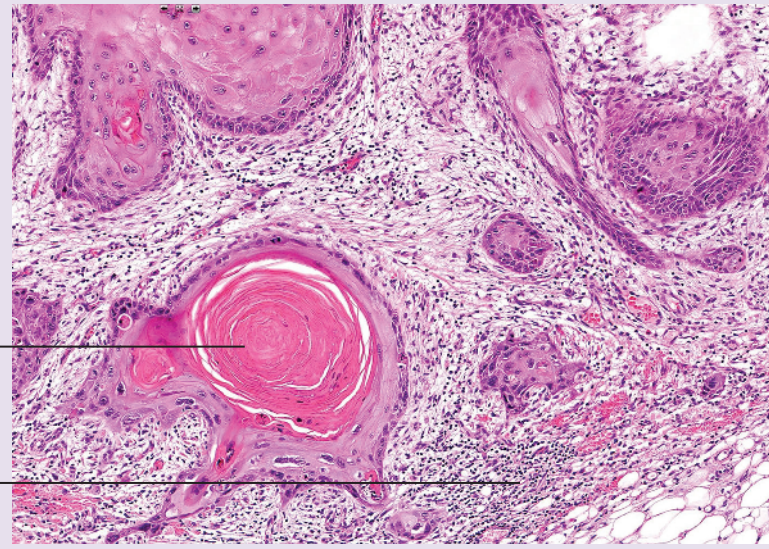






Keratoacanthoma





Hi:

- Symmetrical cup-shaped tumor, filled with cornified debris and with smooth outer margins
- Central keratotic plug with massive acanthosis and papillomatosis
- Bilateral epithelial lip formation of adjacent rete ridges
- Proliferation of atypical keratinocytes and mitoses
- Parakeratosis
- Intraepidermal formation of microabscesses, filled with mixed inflammatory cells and debris
- Mixed cellular infiltrate in the dermis

References

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Misago, N., Takai, T., Toda, S., and Narisawa, Y. (2014) The histopathologic changes in keratoacanthoma depend on its stage. *J Cutan Pathol* **41**(7): 617–19.

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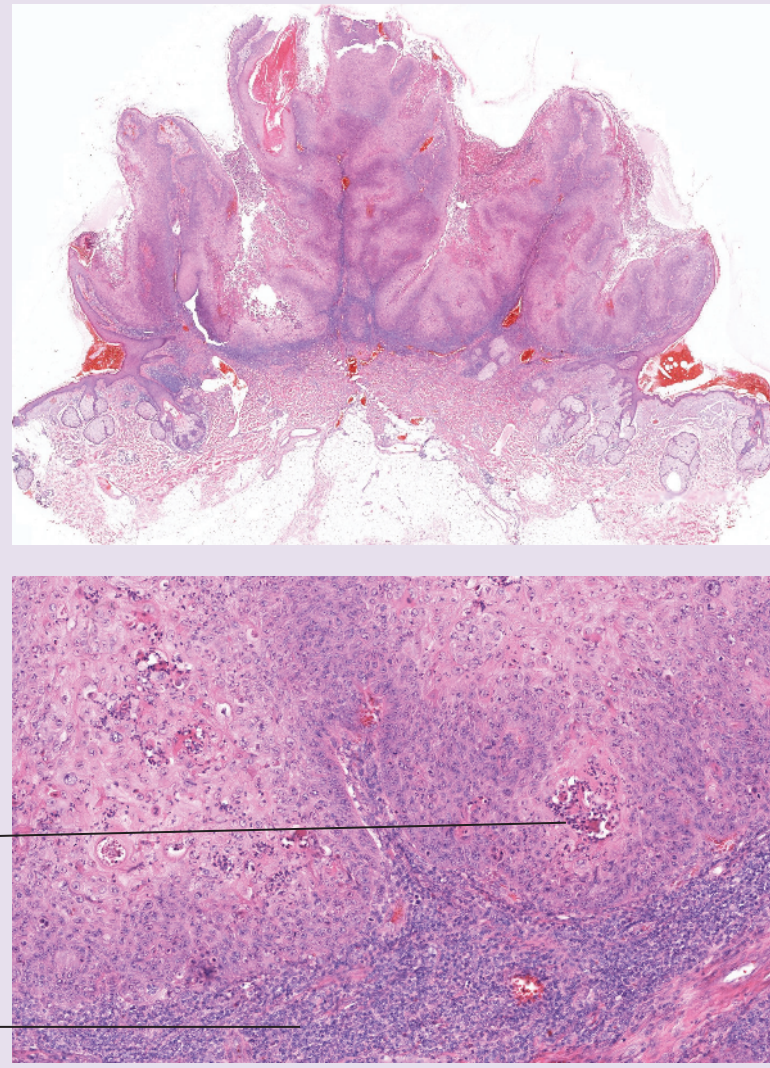
Savage, J.A. and Maize, J.C. Sr (2014) Keratoacanthoma clinical behavior: a systematic review. *Am J Dermatopathol* **36**(5): 422–9.

Epithelioma Cuniculatum (Verrucous Carcinoma) (EC/VC)



Cl: Both exo- and endophytic verrucous lesions, mostly of the soles or perigenital area. Association with HPV infection has been reported.

Hi:

- Exo- or endophytic verrucous hyperkeratosis
- Irregular papillomatosis and acanthosis
- Adjacent epidermis normal
- Well-differentiated keratinocytes
- Low proliferative activity, minimal epithelial dysplasia
- Cysts and sinuses ("fox's burrow"-like), allowing discharge of pus, blood, or cornified debris

DD: Large warts; well-differentiated squamous cell carcinoma.

Comment: Epithelioma cuniculatum/verrucous carcinoma is a genuine carcinoma, albeit lacking the classic histopathological squamous cell carcinoma features, e.g. massive epithelial dysplasia and high proliferative activity. EC/VC is a unique carcinomatous tumor growing by lack of apoptosis rather than by increased proliferation rate. Pathologists should be aware that behind the silhouette of an exo-endophytic epithelial hyperplasia with minimal cytological atypia and scant mitoses, there is a genuine carcinoma.

References

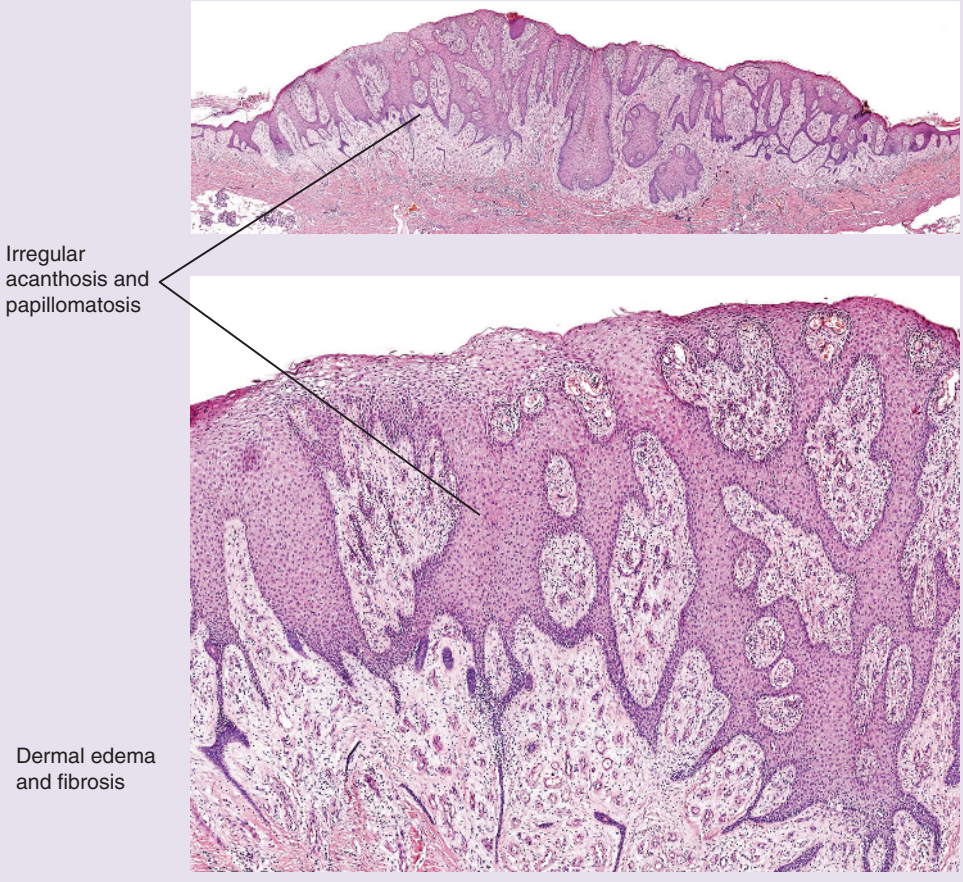
Kubik, M.J. and Rhatigan, R.M. (2012) Carcinoma cuniculatum: not a verrucous carcinoma. *J Cutan Pathol* **39**(12): 1083–7.

Nakamura, Y., Kashiwagi, K., Nakamura, A., and Muto, M. (2015) Verrucous carcinoma of the foot diagnosed using p53 and Ki-67 immunostaining in a patient with diabetic neuropathy. *Am J Dermatopathol* **37**(3): 257–9.

Odar, K., Bostjancic, E., Gale, N., Glavac, D., and Zidar, N. (2012) Differential expression of microRNAs miR-21, miR-31, miR-203, miR-125a-5p and miR-125b and proteins PTEN and p63 in verrucous carcinoma of the head and neck. *Histopathology* **61**(2): 257–65.

Zidar, N., Langner, C., Odar, K., et al. (2017) Anal verrucous carcinoma is not related to infection with human papillomaviruses and should be distinguished from giant condyloma (Buschke–Lowenstein tumour). *Histopathology* **70**(6): 938–45.

Papillomatosis Cutis Carcinoides



Cl: Large, cauliflower-like reactive hyperkeratotic process around chronic inflammatory processes, ulceration or tumor, preferentially on the shins or dorsal aspect of the feet, resembling squamous cell carcinoma.

Hi:

- Irregular acanthosis of pale epithelium with elongation of rete ridges
- Irregular papillomatosis
- Normal keratinocytes
- Edema and fibrosis in the upper dermis
- Variable chronic inflammatory changes of the surrounding tissue

DD: Blastomycosis-like pyoderma.

References

Allerga, F., Manifredi, G., Colli, V., Magnanini, M., and Manfredi, M. (1975) [An uncommon pseudo tumoral skin disease; the so-called Papillomatosis cutis carcinoides. A review (author's transl)]. *Ateneo Parmense Acta Biomed* **46**(6): 649–63.

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Baldauf, K., Strohbach, F., and Laslop, M. (1982) [Malignant transformation of papillomatosis cutis carcinoides Cottron]. *Z Arztl Fortbild (Jena)* **76**(1–2): 69–71.

Bues, M., Muller, K.M., and Schwering, H. (1983) [Pseudocancer of the skin following lower leg amputation. Rare case of Gottron's papillomatosis cutis carcinoides]. *Zentralbl Chir* **108**(14): 895–9.

Cajkovac, V., Trbuljak, M., and Petricic, B. (1970) [Papillomatosis cutis carcinoides Gottron]. *Rad Med Fak Zagrebu* **18**(1): 81–7.

Rathjens, B. (1953). [Papillomatosis cutis carcinoides Gottron]. *Dermatol Wochenschr* **127**(14): 313–17.

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Florid Papillomatosis of the Oral Cavity (Oral Verrucous Carcinoma)

Cl: Whitish cobblestone-like plaques and papules of the buccal mucosa. Lesions may progress to cauliflower-like exophytic neoplasms.

Hi:

- Hyperplastic epithelial layer
- Focal granulosis and slight parakeratosis
- No significant proliferative activity

DD: Hairy leukoplakia occurs mostly in immunocompromised patients, preferentially at the lateral margins of the tongue, presenting with poorly circumscribed whitish plaques similar to hyperplastic leukoplakia. Histopathologically, there is a typical zonation or "tricolore" pattern with superficial eosinophilic parakeratosis in conjunction with a verrucous surface, a midepithelial pale zone of ballooned keratinocytes, and a basal zone of eosinophilic banal epithelia. EBER *in situ* hybridization shows Epstein–Barr virus in the superficial layer. There may be HPV co-infection.

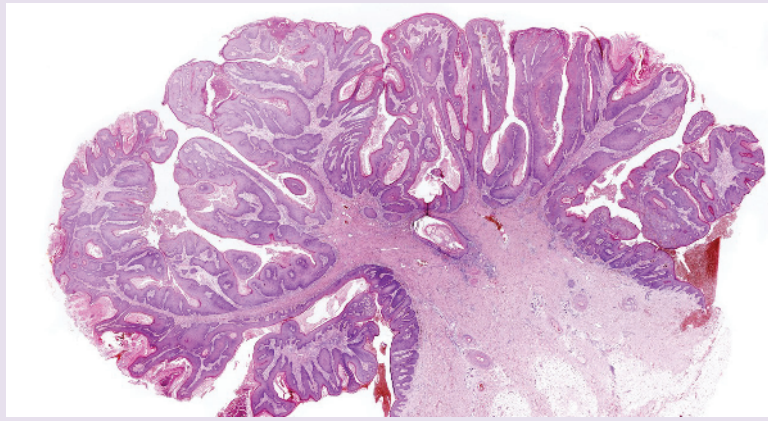
References

Collangettes, D., Chollet, P., and Fonck, Y. (1993) Oral florid papillomatosis. *Eur J Cancer B Oral Oncol* **29B**(1): 81–2.

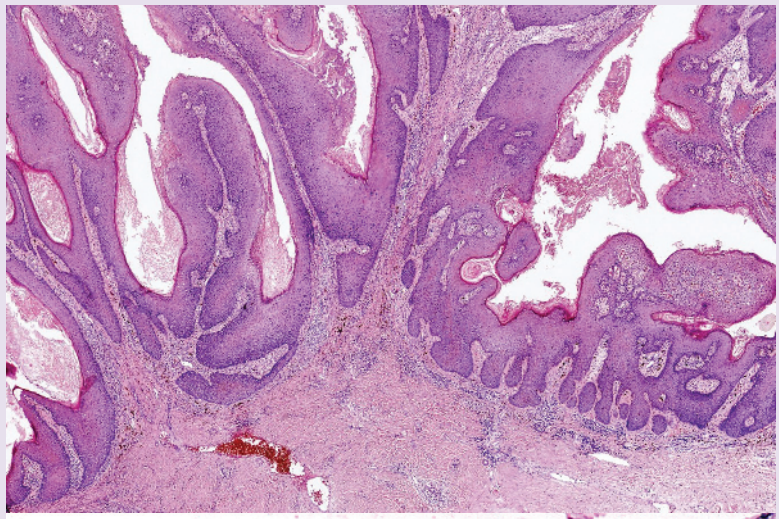
Grillo, E., Miguel-Morrondo, A., Vano-Galvan, S., and Jaen-Olasolo, P. (2012) [Oral florid papillomatosis]. *Rev Clin Esp* **212**(11): e93.

Perez-Belmonte, L.M., Gomez-Moyano, E., Herrero-Lifona, L., and Jimenez-Onate, F. (2015) [Verrocous mass on the tongue: oral florid papillomatosis]. *Enferm Infecc Microbiol Clin* **33**(2): 135–6.

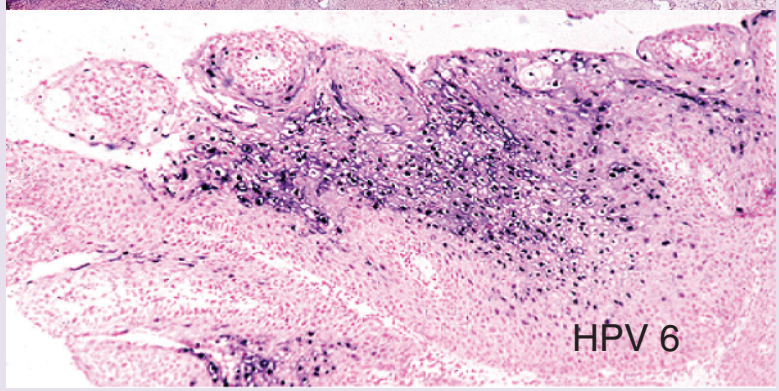
Buschke–Löwenstein Tumor (Giant Condyloma)



Exophytic lesion, showing verruciform acanthosis and papillomatosis



HPV6 In-situ hybridization



BOWEN'S DISEASE

Cl: Large, almost cerebriform, foul-smelling papillomatous tumor, evolving from recurring and progressing small genital or perianal lesions.
Hi: Large condyloma, epithelial proliferation and dysplasia.

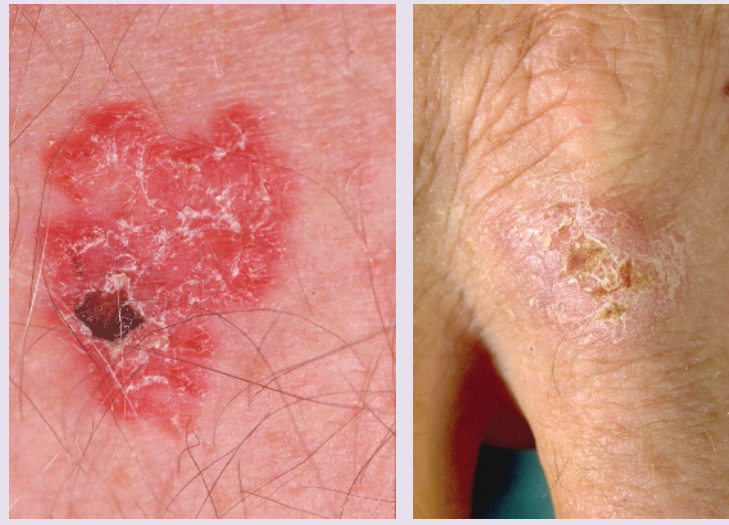
Reference

Zidar, N., Langner, C., Odar, K., et al. (2017) Anal verrucous carcinoma is not related to infection with human papillomaviruses and should be distinguished from giant condyloma (Buschke–Lowenstein tumour). *Histopathology* **70**(6): 938–45.

Malignant Epidermal Neoplasms

Bowen's Disease (Carcinoma *in situ*)

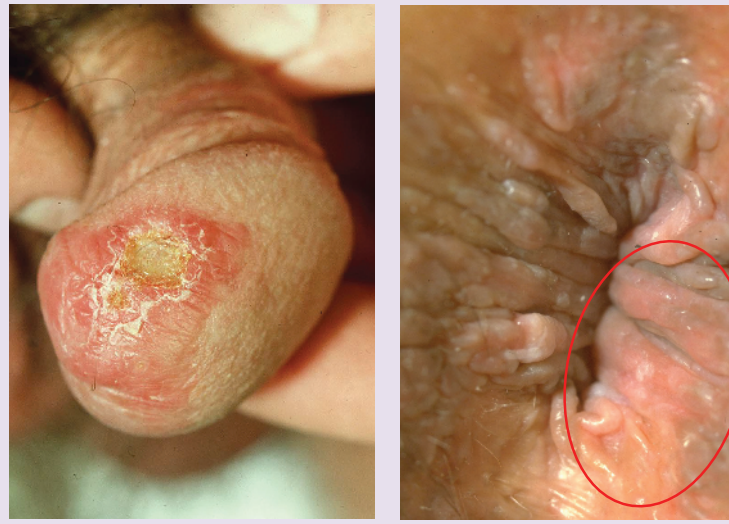
Psoriasiform and keratotic plaque on the trunk (left) and finger (right) respectively



Erythroplasia (Queyrat)

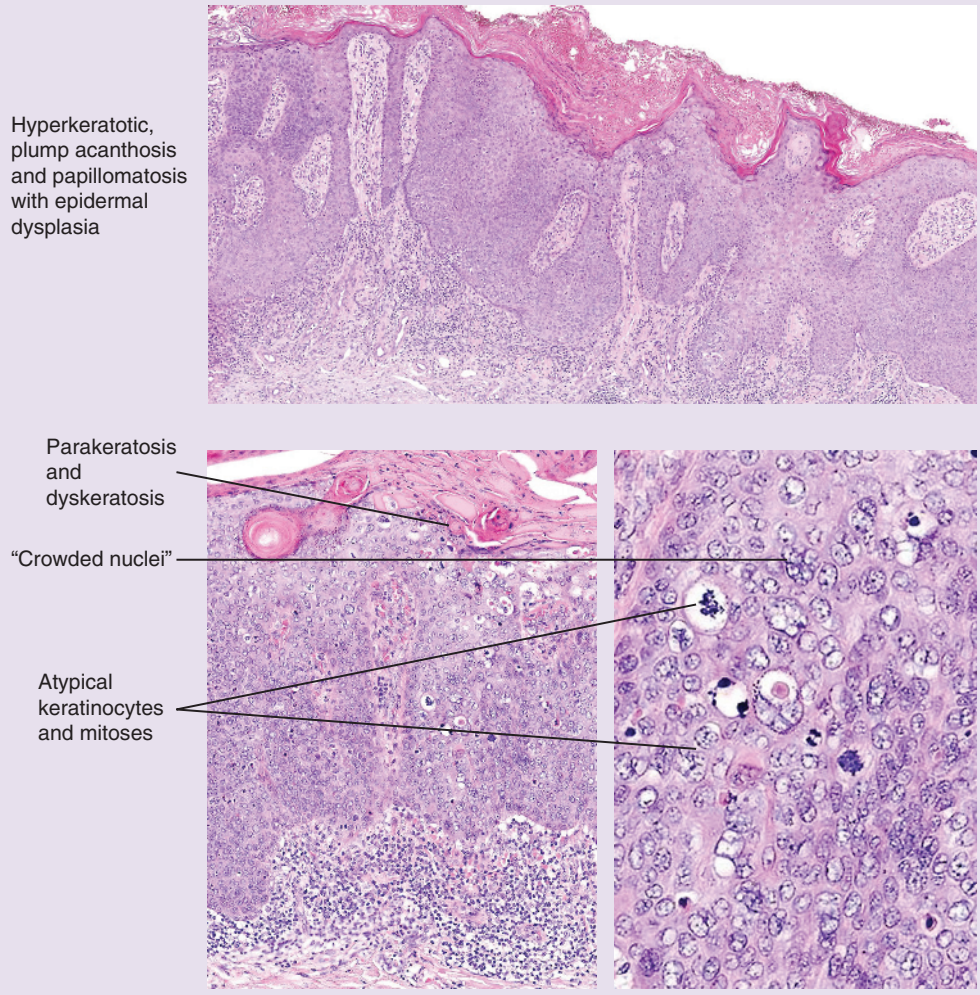
Sharply demarcated irregular plaque on the glans penis

Plaque in the perianal region without sharp demarcation (circle)



BOWEN'S DISEASE

Bowen's Disease



Cl: Flat, slowly expanding, psoriasiform, sharply bordered red or pink patch or plaque most frequently located on the trunk, but also at any other site of the body. Variants are erythroplasia of Queyrat at the male genitalia or pigmented Bowen's disease, preferentially in the anogenital region; the latter is often associated with HPV16/18 infection. Bowen's disease of the nailbed may be easily misdiagnosed.

Hi:

- Parahyperkeratosis and plump acanthosis
- The hallmarks are large, atypical, occasionally dyskeratotic multinucleated keratinocytes and many atypical mitotic figures, disseminated over all levels of the epidermis
- "Crowded nuclei"
- Preservation of a regular basal layer
- The tumor is *in situ* and does not cross the basement membrane. Invasive variants correspond to Bowen's carcinoma
- Tumor invasion into the epithelium of hair follicles and sweat glands may occur
- Clear cell type of Bowen's disease with multiple PAS-positive tumor cells may simulate Paget's disease

DD: Bowenoid actinic keratosis; bowenoid papulosis; superficial spreading melanoma; clonal seborrheic keratosis; pigmented Paget's disease of the mamilla.

BOWEN'S DISEASE

References

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Idriss, M.H., Misri, R., and Boer-Auer, A. (2016) Orthokeratotic Bowen disease: a histopathologic, immunohistochemical and molecular study. *J Cutan Pathol* **43**(1): 24–31.

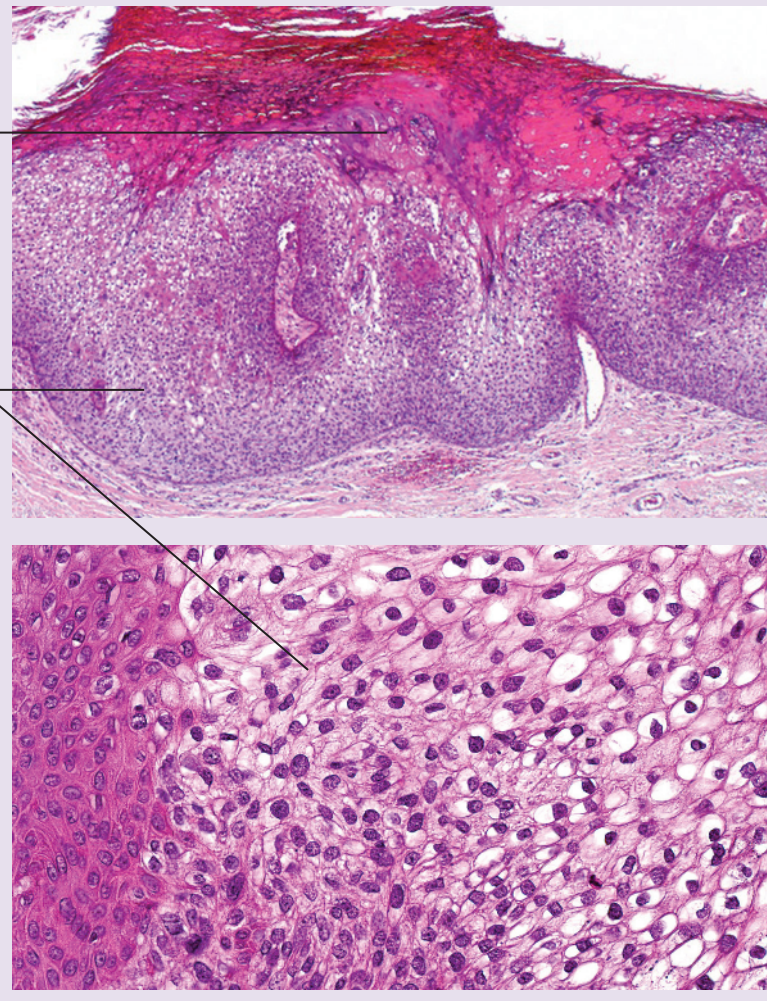
Kalegowda, I.Y. and Boer-Auer, A. (2017) Clonal seborrheic keratosis versus pagetoid bowen disease: histopathology and role of adjunctive markers. *Am J Dermatopathol* **39**(6): 433–9.

Kogut, M., Toberer, F., Enk, A.H., and Hassel, J.C. (2016) Limitations of Ber-EP4 for distinction of Bowen disease from basal cell carcinoma. *J Cutan Pathol* **43**(4): 367–71.

Svajdler, M. Jr, Mezencev, R., Kaspirkova, J., et al. (2016) Human papillomavirus infection and p16 expression in extragenital/extraungual bowen disease in immunocompromised patients. *Am J Dermatopathol* **38**(10): 751–7.

Takayama, R., Ishiwata, T., Ansai, S., et al. (2013) Lumican as a novel marker for differential diagnosis of Bowen disease and actinic keratosis. *Am J Dermatopathol* **35**(8): 827–32.

Variant: Clear Cell Bowen's Disease

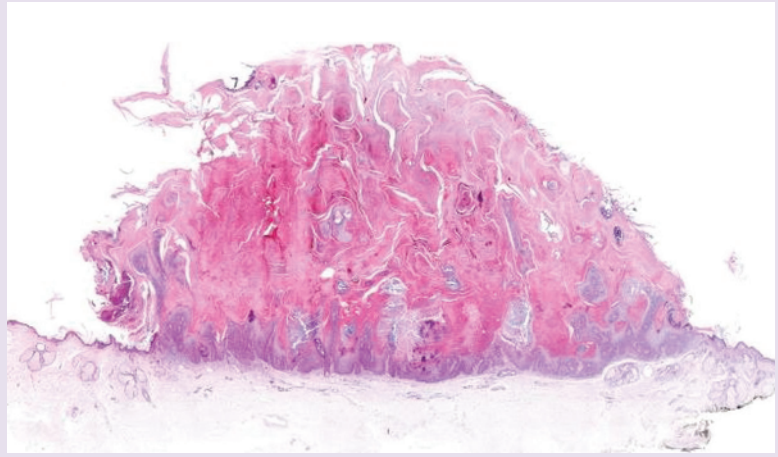


BOWEN'S DISEASE

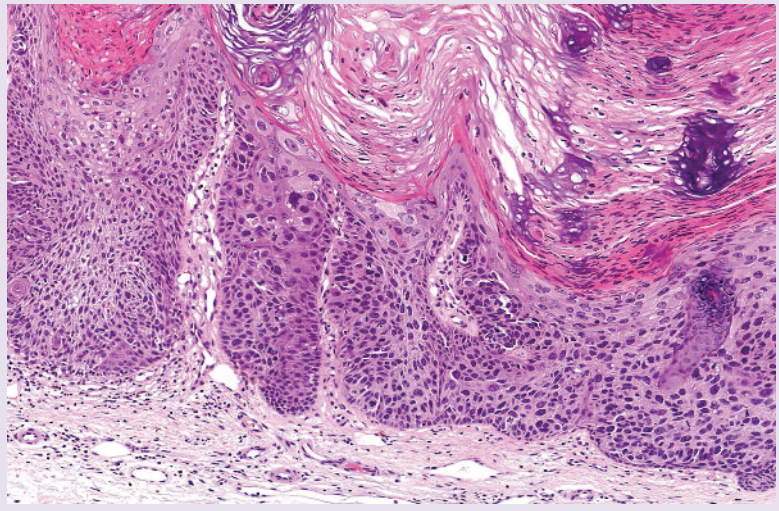
Hi: Pale keratinocytes with PAS-positive glycogen-rich cytoplasm.

Variant: Cutaneous Horn (Cornu Cutaneum) on Bowen's Disease

Pyramid-like hyperkeratosis



Bowen's disease (carcinoma in-situ) underlying cutaneous horn



Cl: Morphological term, describing a keratotic exophytic tumorous lesion, originating from various conditions, including Bowen's disease, actinic keratosis, squamous cell carcinoma.

Hi:

- Pyramid-shaped hyperkeratosis
- At the base histological features of Bowen's disease

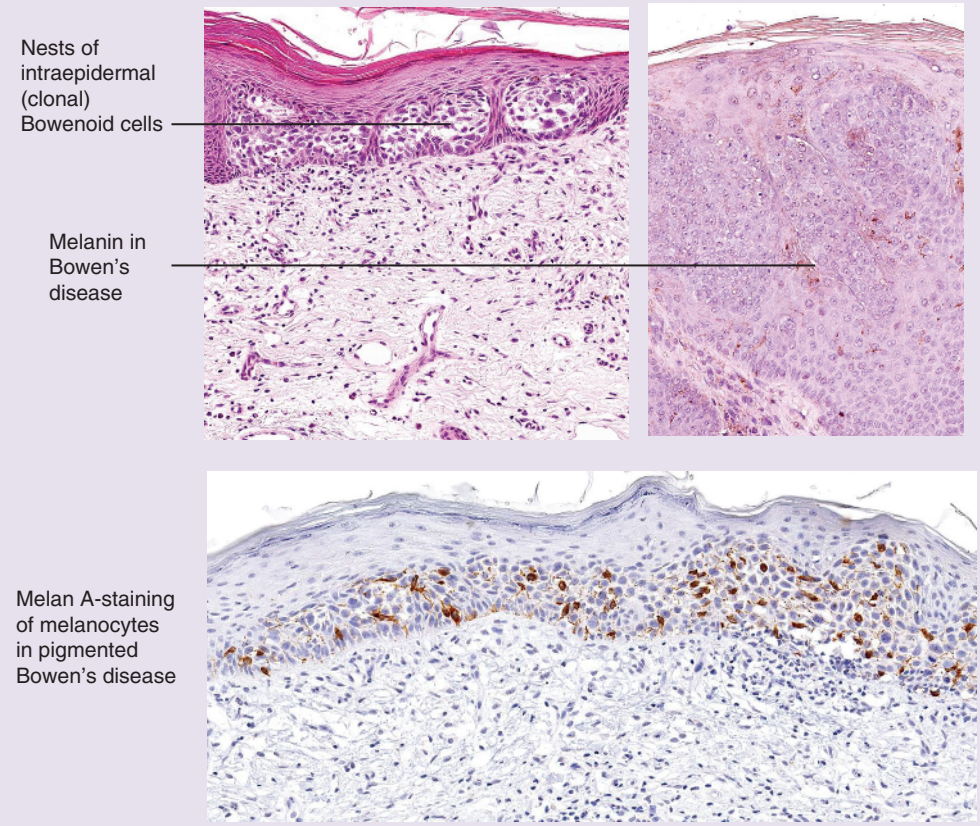
DD: Cutaneous horn on actinic keratosis; warty dyskeratoma; squamous cell carcinoma; lupus erythematosus.

BOWEN'S DISEASE

Reference

Lora, V., Scarabello, A., and Cota, C. (2015) Warty dyskeratoma as a cutaneous horn of the mons pubis. *Am J Dermatopathol* **37**(10): 802–4.

Variant: Pigmented (Anogenital) and Clonal Bowen's Disease



Cl: Bowen's disease in the anogenital region frequently is pigmented, especially in dark-skinned individuals. Most cases are associated with oncogenic HPV infection (HPV16, HPV18).

Hi:

- Hyperpigmented bowenoid keratinocytes
- Atypical keratinocytes are AE1/AE3 positive but CK7 negative
- Slightly increased number of Melan A-positive melanocytes

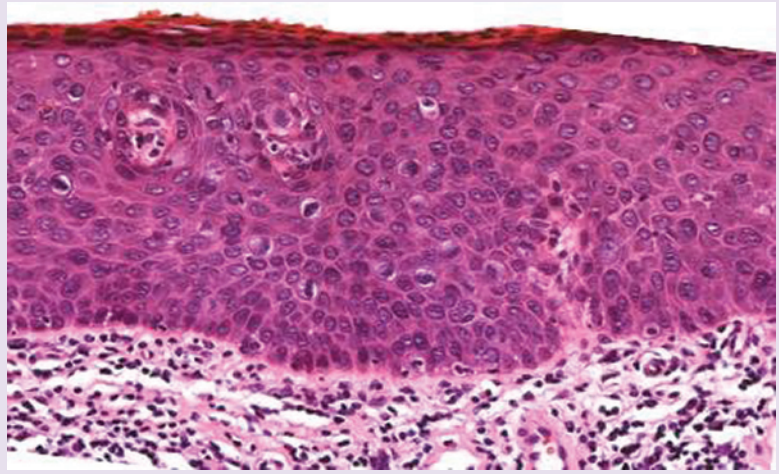
BOWEN'S DISEASE

Variant: Erythroplasia of Queyrat and Vulvar Intraepithelial Neoplasia

Glans penis

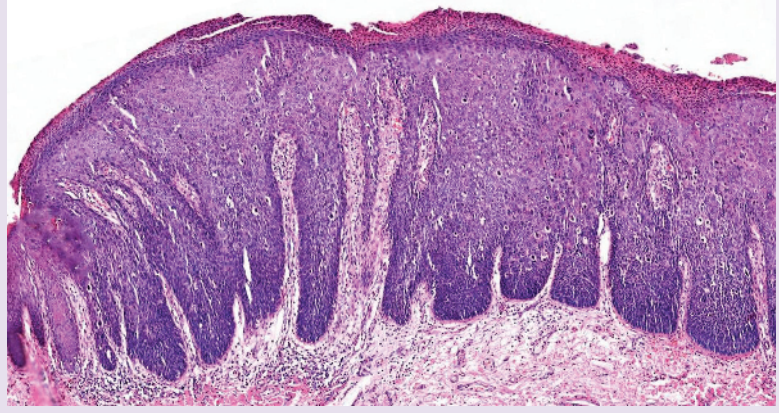
Acanthosis, bowenoid cells in all levels of the epidermis

Inflammatory infiltrate, containing many plasma cells

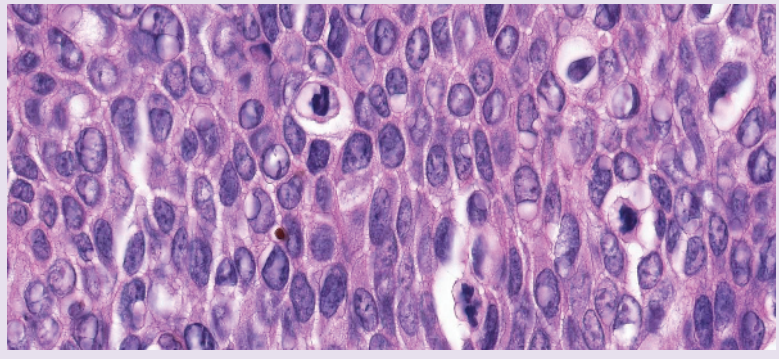


Vulva

Acanthosis, papillomatosis



Bowenoid cells with marked pleomorphism and mitoses



BASAL CELL CARCINOMA

Cl: Red, velvety, sharply bordered irregular patch or plaque on the glans penis. Similar lesions can be found in anogenital localisations and oral mucosa of both sexes. By some authors, Queyrat's disease is considered to be a separate entity with a worse prognosis rather than a variant of Bowen's disease.
Hi:

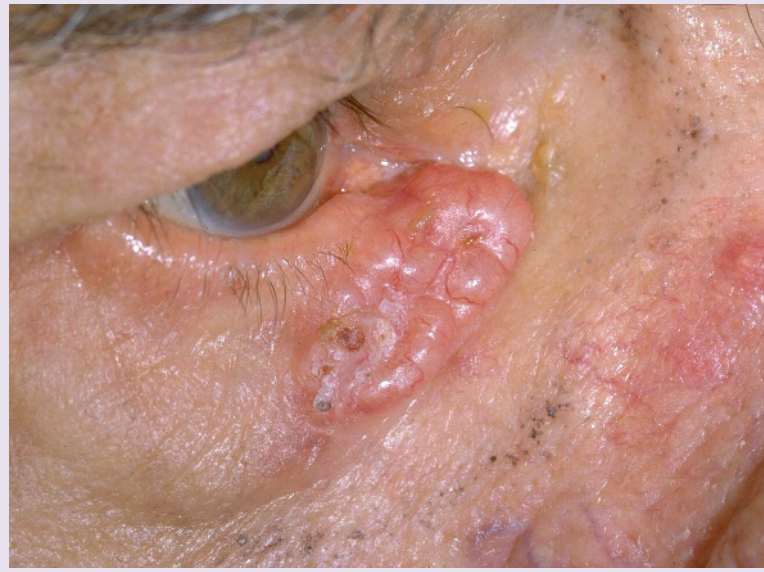
- Superficial erosion
- Slight acanthosis and/or papillomatosis
- Minimal dyskeratosis
- Atypical "bowenoid" keratinocytes in all levels of the epidermis
- Inflammatory infiltrate on the basis of the lesion, containing many plasma cells

Basal Cell Carcinoma (BCC)

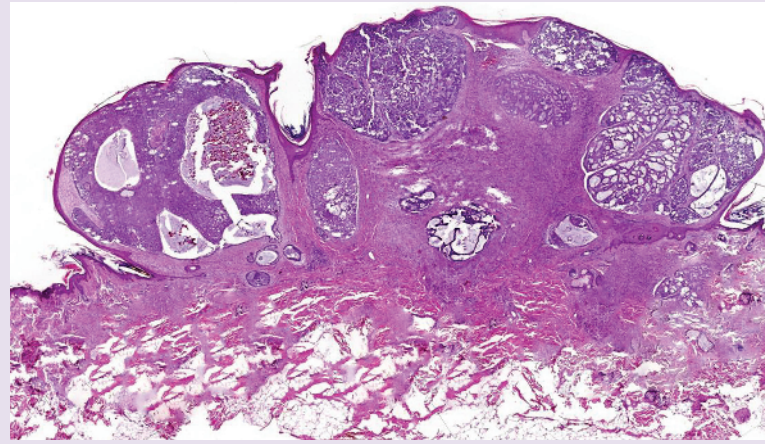
Many variants exist.

Variant: Nodular BCC

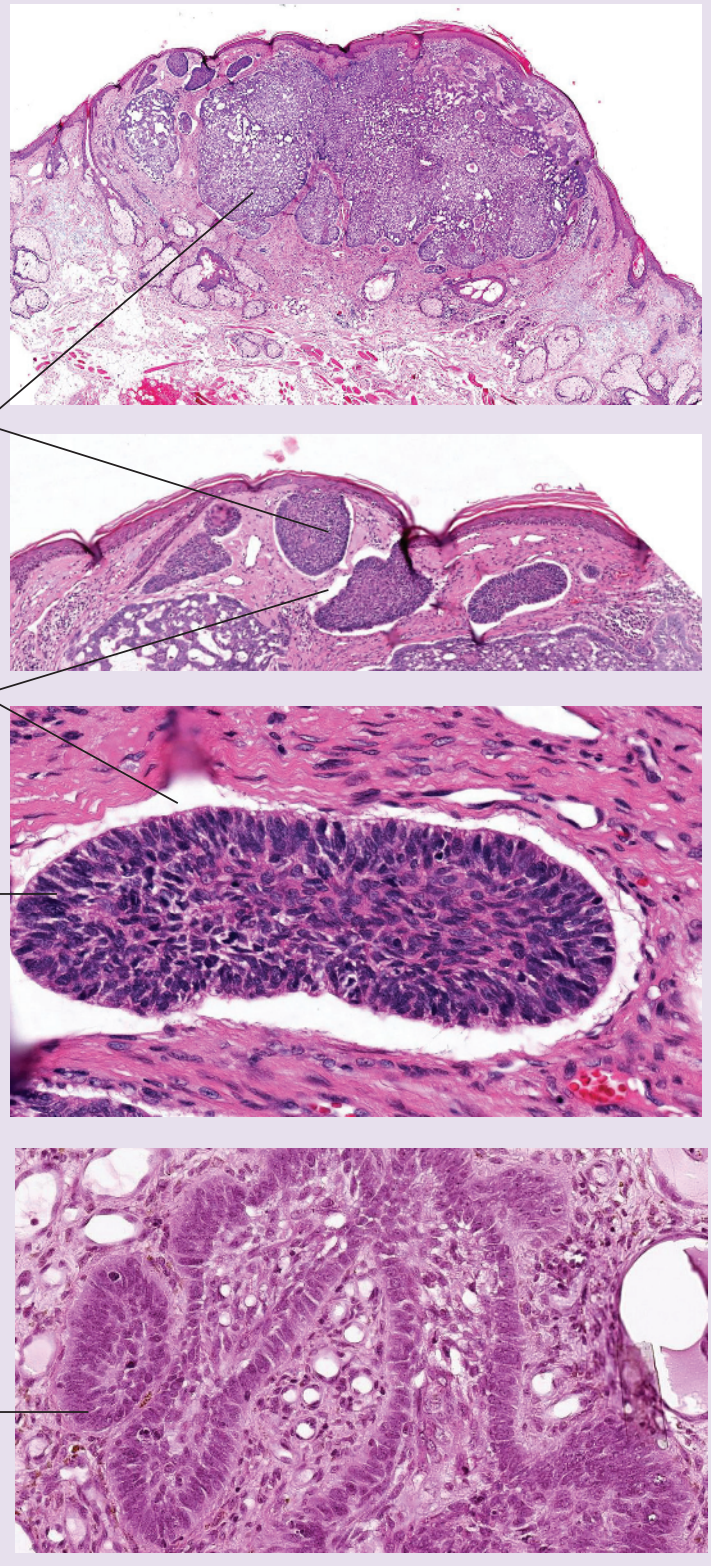
Pearly, waxy tumor with elevated border and telangiectases



Exophytic proliferation of basaloid cells



Variant: Nodular BCC

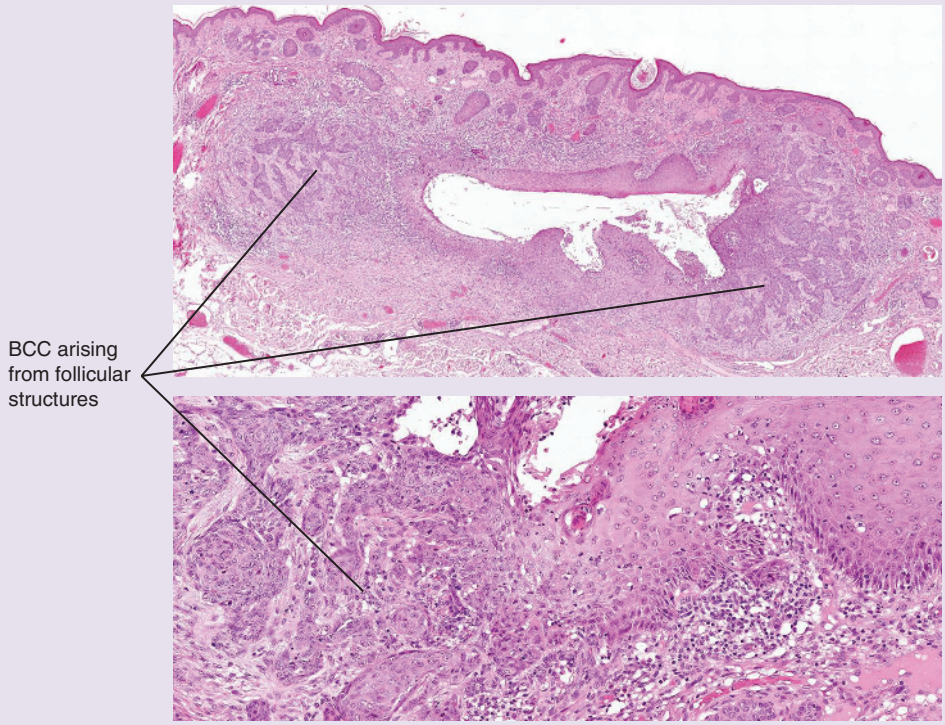


BASAL CELL CARCINOMA

Cl: Pink or red well-circumscribed nodule, preferentially localized in sun-exposed skin. Pearly or waxy elevated border, telangiectases. Often central superficial erosion and crust formation.
Hi:

- Basophilic roundish and oval-shaped epithelial cells
- Peripheral band-like palisading arrangement
- Connection between tumor and epidermis or adnexa
- Prominent shrinkage clefts between tumor and surrounding stroma
- Immunohistochemical expression of BerEP4

Variant: Infundibulocystic BCC



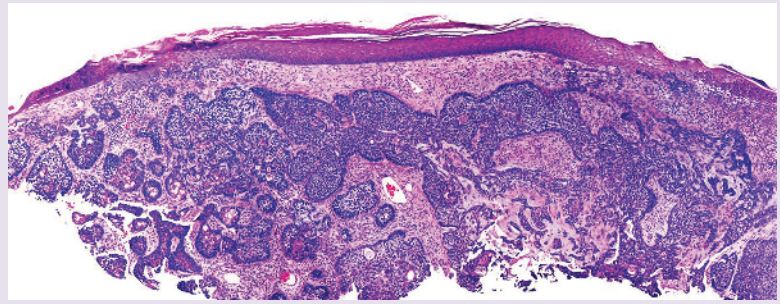
Cl: No specific clinical appearance.

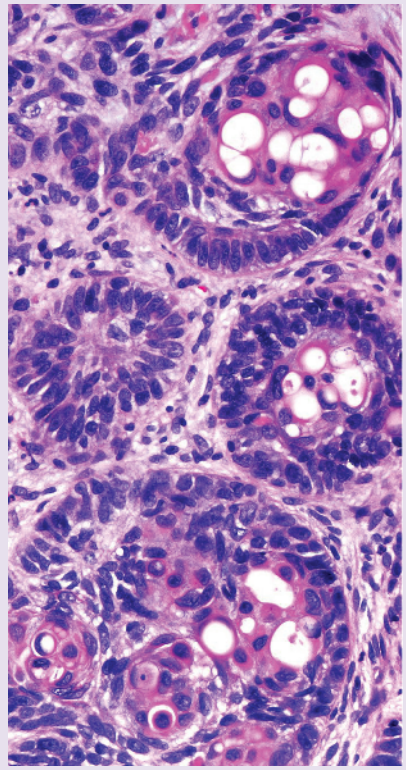
Hi: Proliferation of basaloid cells, originating from follicular structures.

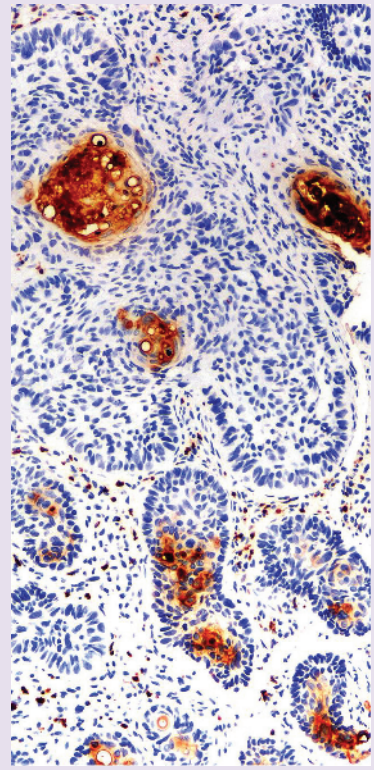
BASAL CELL CARCINOMA

Variants of BCC With Ductal, Matrical or Sebaceous Differentiation

Variant: BCC with Ductal Differentiation







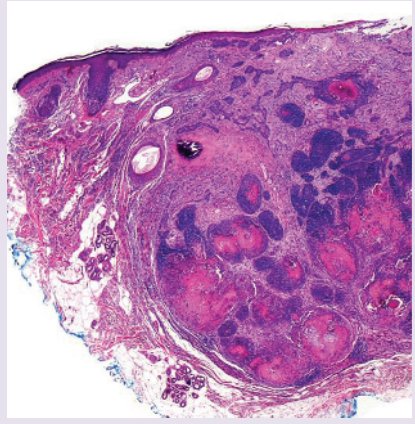
BCC with ductal structures; CEA-positive

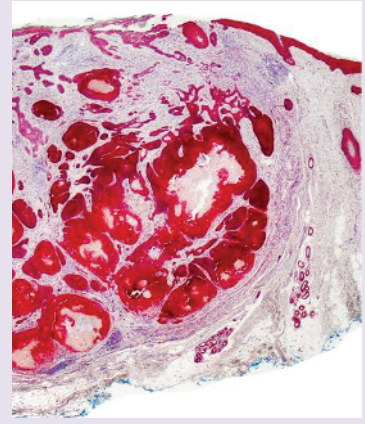
Courtesy of Luis Requena, Madrid

BASAL CELL CARCINOMA

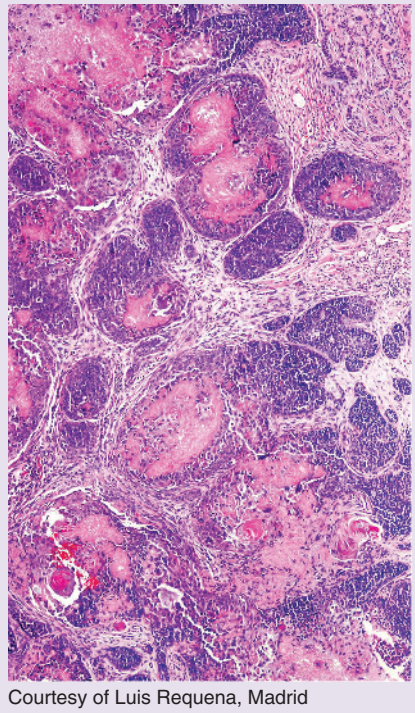
Variant: BCC with Matrical Differentiation

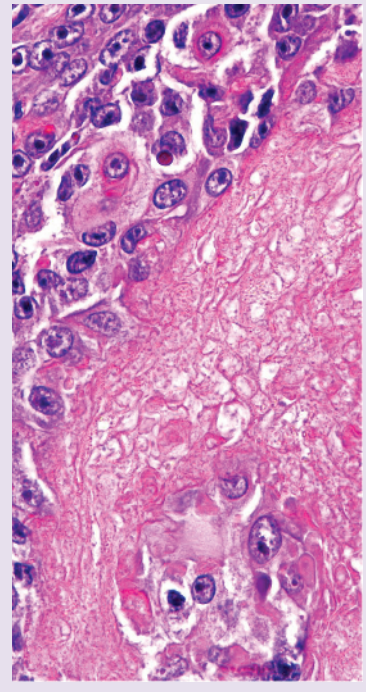
BCC with matrical differentiation; beta-catenin (right)





Nests of basaloid cells; shadow cells (right)



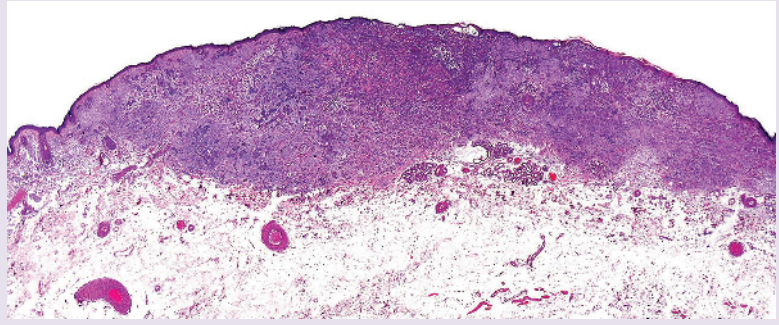


Courtesy of Luis Requena, Madrid

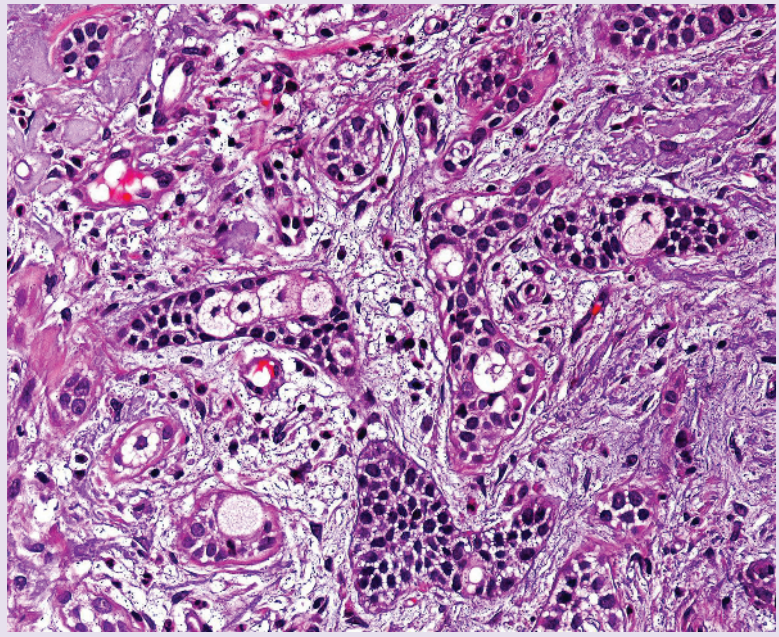
BASAL CELL CARCINOMA

Variant: BCC with Sebaceous Differentiation

BCC with strong fibrous stroma reaction



Nests of basaloid cells with sebaceous differentiation



Courtesy of Luis Requena, Madrid

Comment: Distinct differentiation towards various structures may be seen in some BCC, which sometimes leads to diagnostic pitfalls.

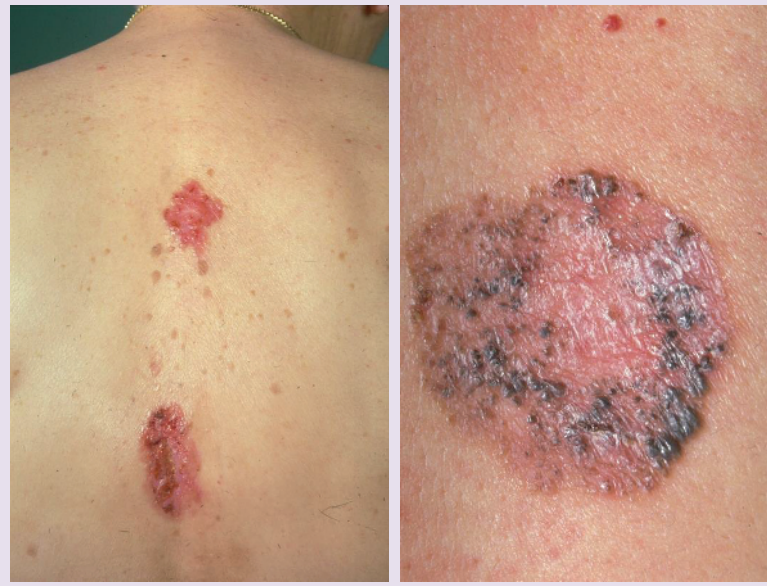
References

Ambrojo, P., Aguilar, A., Simon, P., Requena, L., and Sanchez Yus, E. (1992) Basal cell carcinoma with matrical differentiation. *Am J Dermatopathol* **14**(4): 293–7.

Del Sordo, R., Cavaliere, A., and Sidoni, A. (2007) Basal cell carcinoma with matrical differentiation: expression of beta-catenin [corrected] and osteopontin. *Am J Dermatopathol* **29**(5): 470–4.

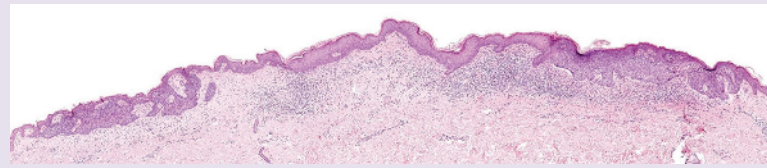
BASAL CELL CARCINOMA

Variant: Superficial BCC

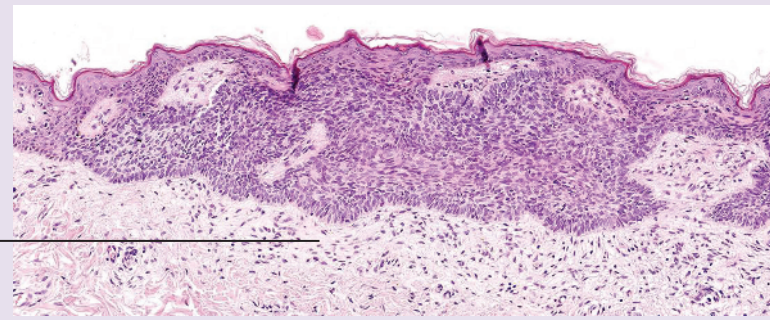


Left: multiple superficial BCCs

Right: pigmented superficial BCC



Multicentric nests attached to the epidermis



Superficial BCC

Mucin in the surrounding stroma

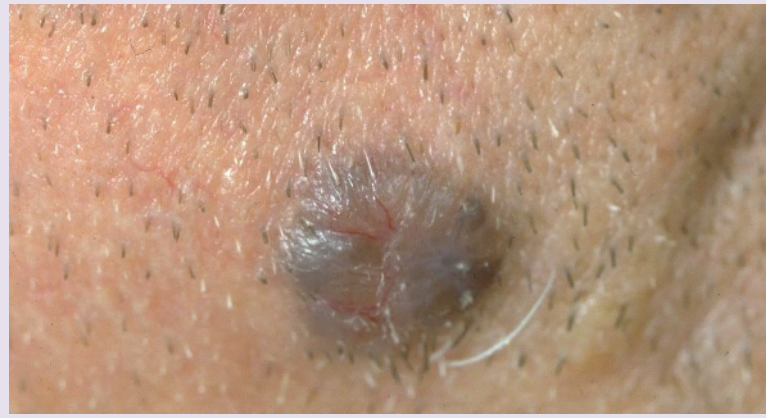
Cl: Solitary or multiple plaques; mostly located on the trunk.

Hi:

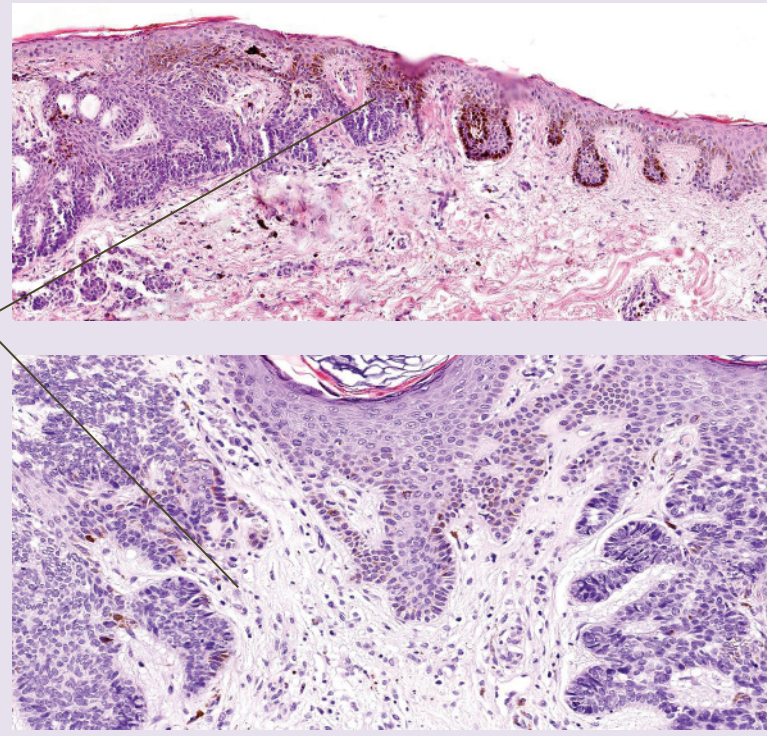
- Solitary or confluent superficial nests of basaloid epithelial cells
- Connection with the epidermis or with adnexal structures
- Peripheral palisading
- Distinct shrinkage clefts
- Adjacent tumor stroma containing mucin
- Fibrosis and inflammatory infiltrate in the upper dermis

BASAL CELL CARCINOMA

Variant: Pigmented BCC



Pigmented nodular BCC



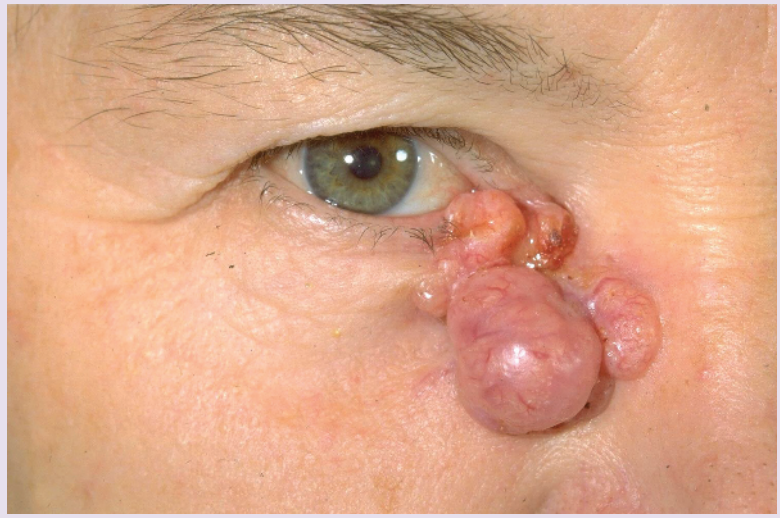
Melanin deposits in basaloid cells and in melanophages in the surrounding stroma

Cl: Nodular or superficial pigmented lesion.
Hi: Increased number of intratumoral melanocytes in scattered array.

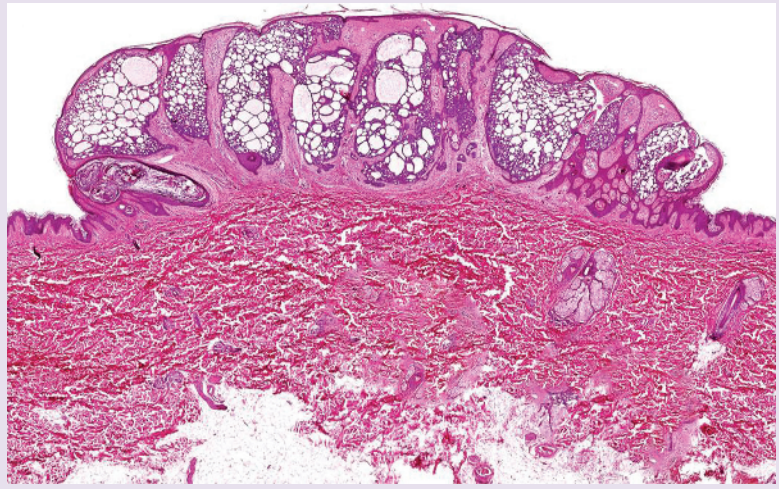
BASAL CELL CARCINOMA

Variant: Adenoid-Cystic BCC

Adenoid-cystic BCC, originating from the lower eyelid



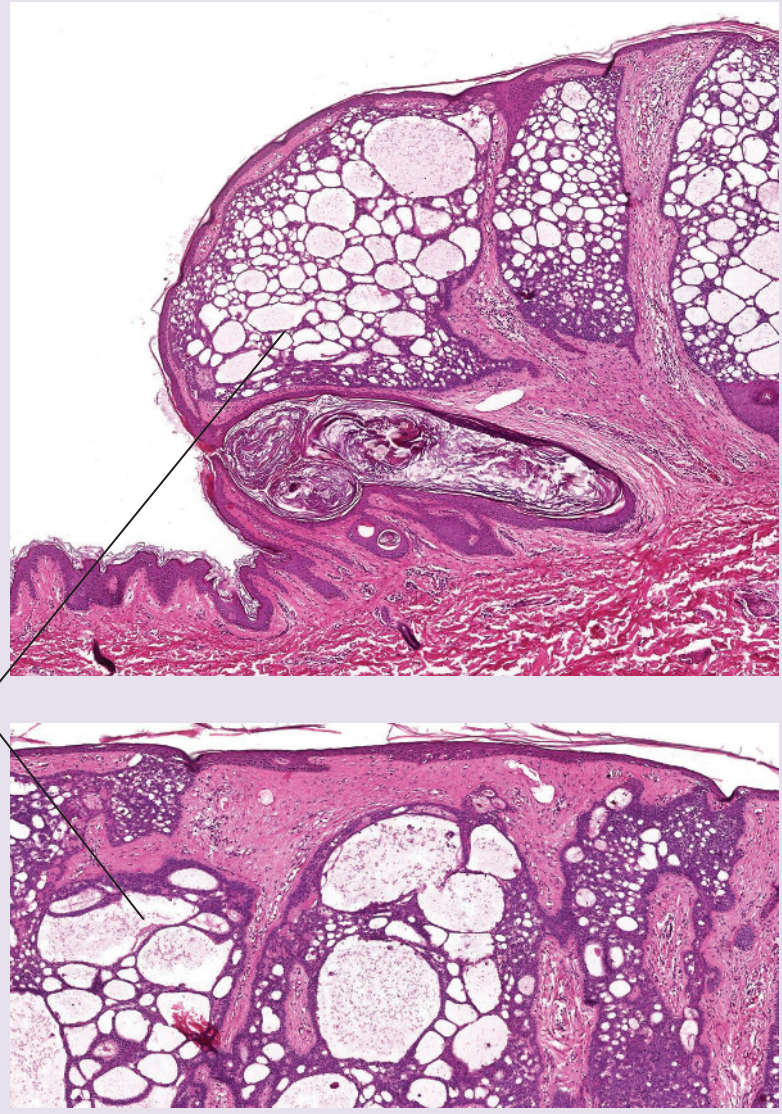
Tumor from the trunk. Fenestrated tumor pattern. Intralesional cystic spaces



Cl: Single or multiple confluent soft, translucent bluish-white nodules with discrete telangiectases. Preferential localisation is the eyelids. Hidrocystoma is the most common differential diagnosis.
Hi: Solid nodules of basaloid cells and intratumoral mucin-filled cystic spaces.
DD: Mucinous eccrine carcinoma, showing slender strands of basaloid epithelial cells lying in "puddles of mucin." Endocrine mucin-producing tumor (as a variant of mucinous eccrine carcinoma) presenting with roundish basaloid tumor nests in a "cannonball"-like arrangement. Nests may contain intratumoral mucinous lakes. Characteristic immunophenotype with expression of chromogranin, synaptophysin, estrogen, and progesterone.

BASAL CELL CARCINOMA

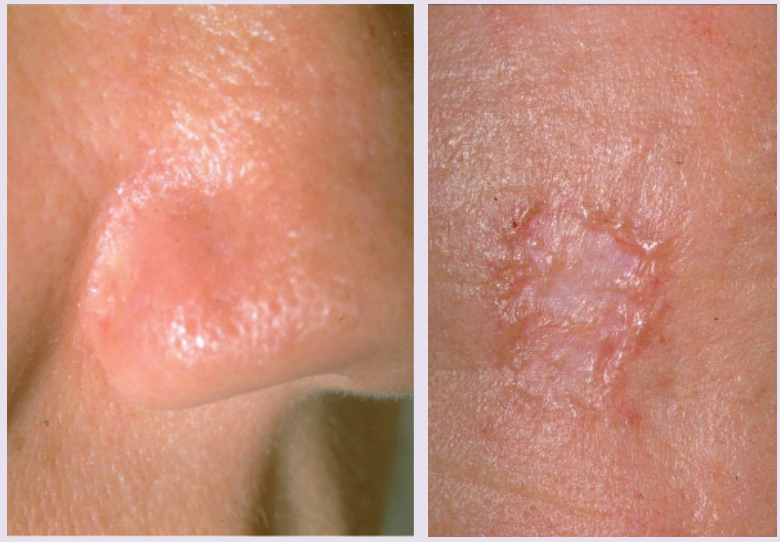
Variant: Adenoid-Cystic BCC



BASAL CELL CARCINOMA

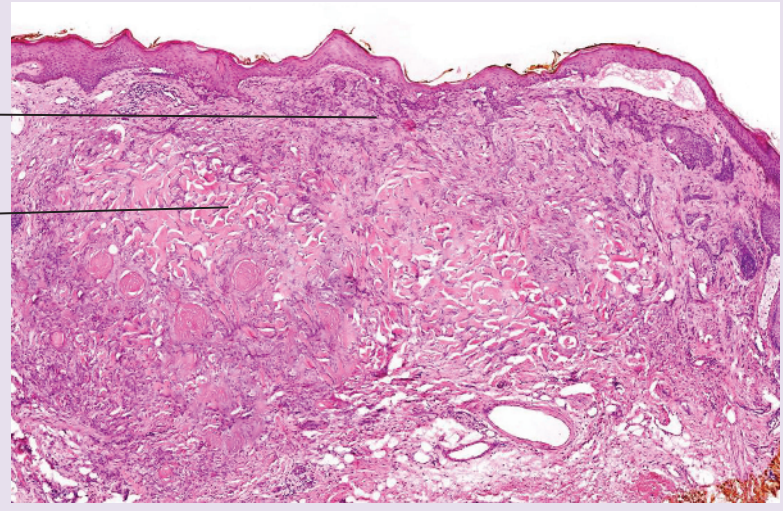
Variant: Sclerodermiform (Morpheaform) BCC

Slightly atrophic superficial lesions on the nose (left) and forehead (right)



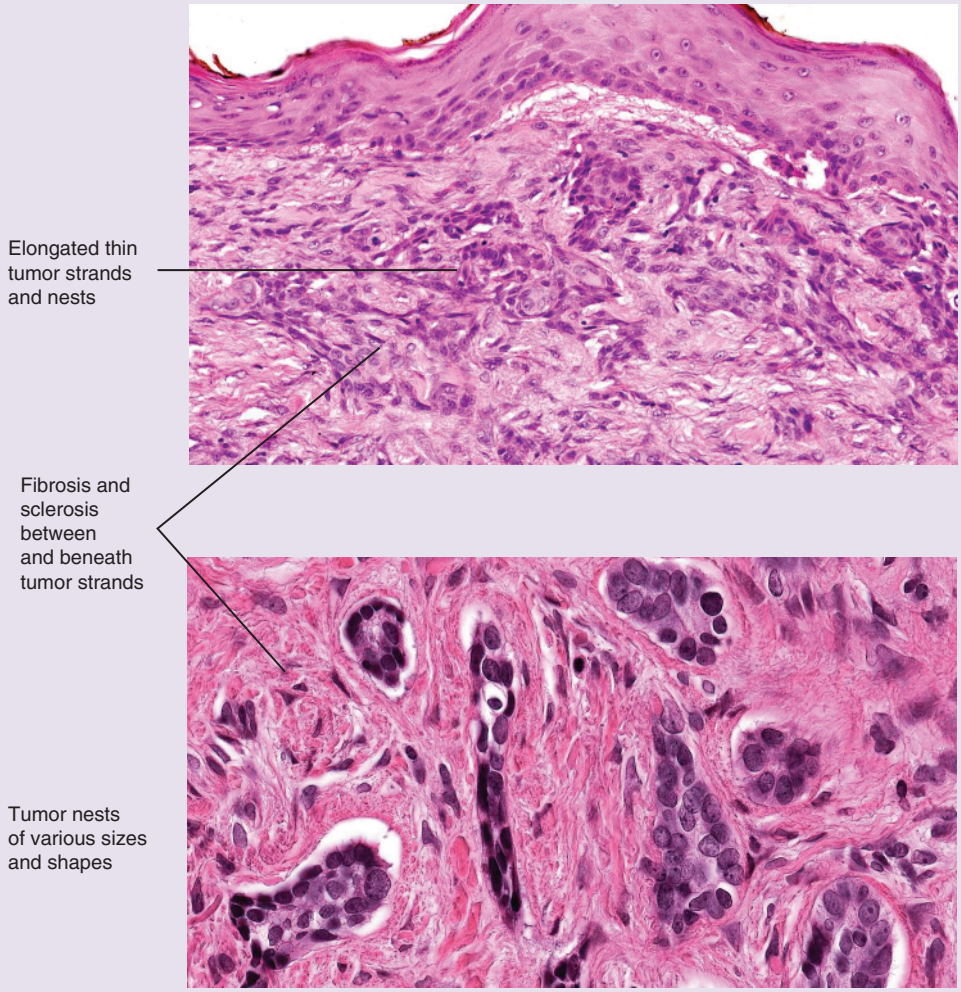
Delicate tumor strands within sclerotic stroma

Sclerosis between and underneath tumor islands



BASAL CELL CARCINOMA

Variant: Sclerodermiform (Morpheaform) BCC



Cl: Poorly circumscribed indurated scar-like lesion. Spread beyond clinically recognizable borders. Aggressive course, especially in the nasolabial fold, where deeper structures may be involved. Ulceration is rare.

Hi:

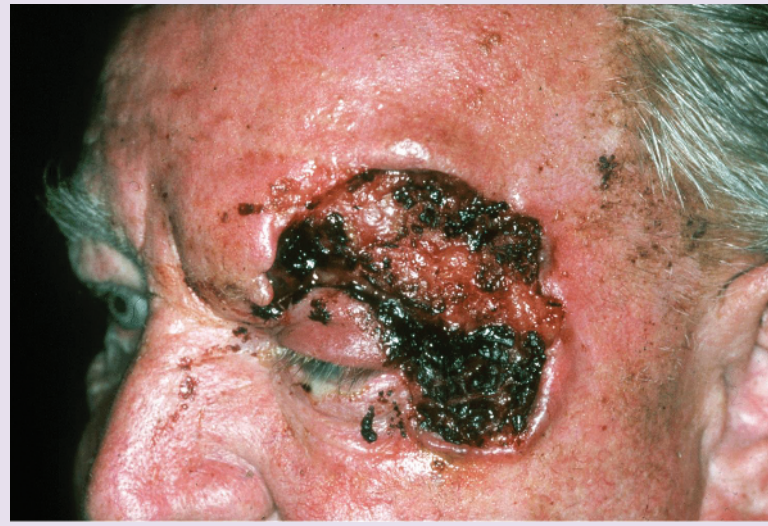
- Small thin tumor islands and strands, proliferating between collagen bundles
- Absence of peripheral palisading
- Fibrosis of the surrounding dermis
- Cleft formation may occur, but is not typical
- Strong positivity for BerEP4

DD: Clinical differential diagnoses include traumatic scar, morphea, desmoplastic melanoma, desmoplastic trichoepithelioma, microcystic adnexal carcinoma.

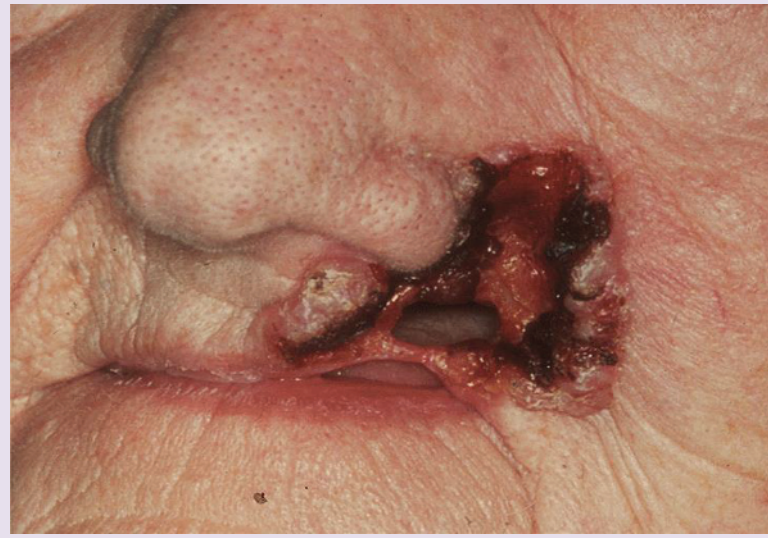
BASAL CELL CARCINOMA

Clinical Variants: Ulcerating BCCs

Ulcus rodens



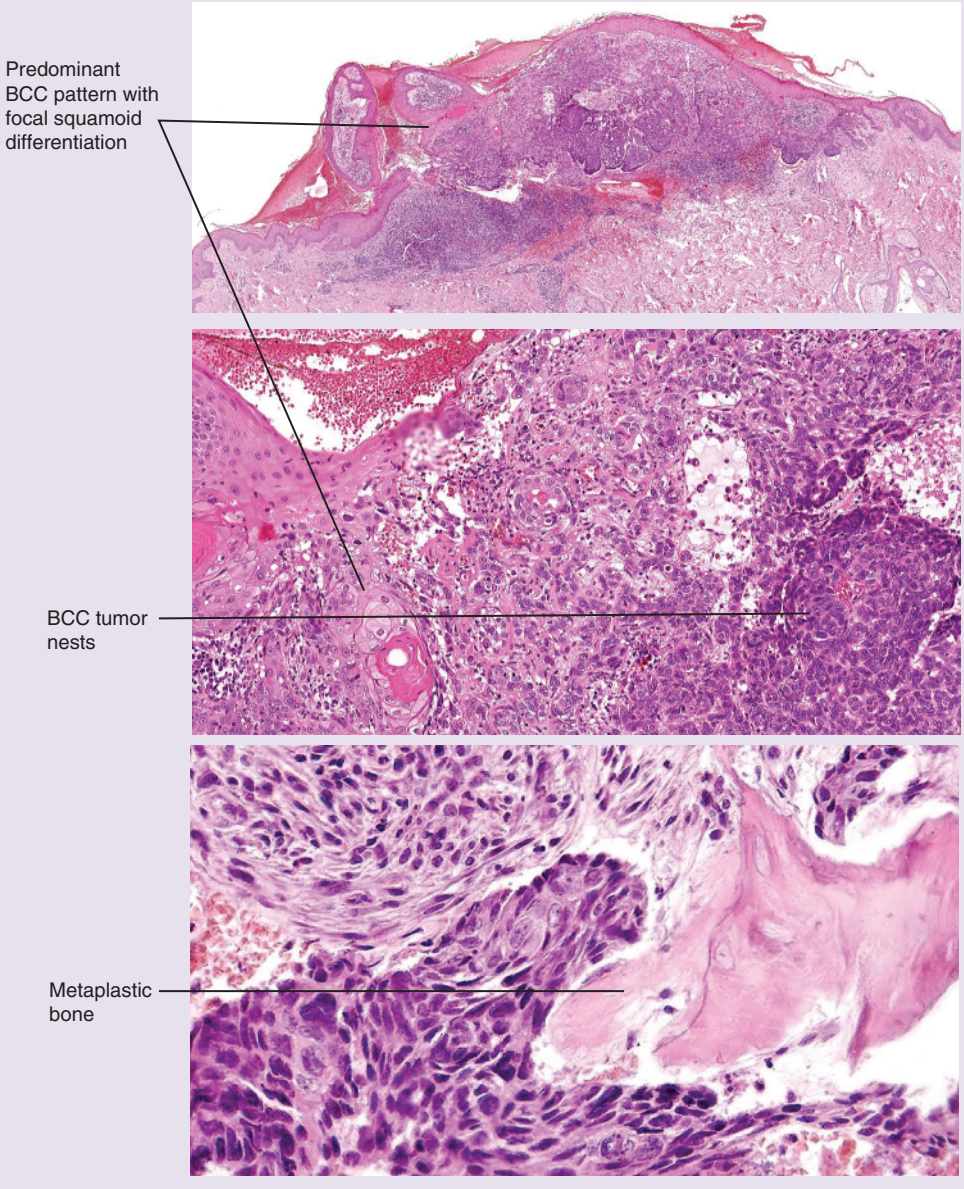
Ulcus terebrans



Two types can be differentiated, both with an aggressive clinical course. Ulcus rodens ulcerates and spreads peripherally, whereas ulcus terebrans spreads into the depth, destroying underlying structures, including cartilage and bone.

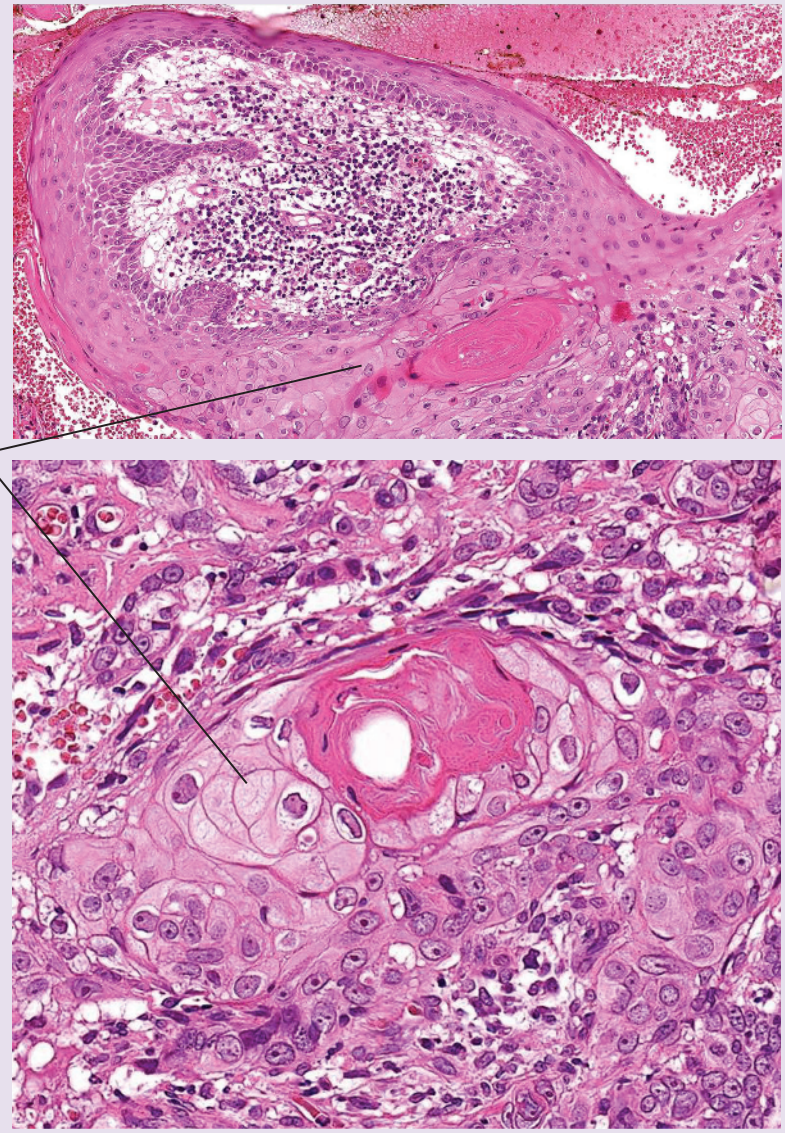
BASAL CELL CARCINOMA

Histological Variants: Metatypic BCC with Squamoid Differentiation



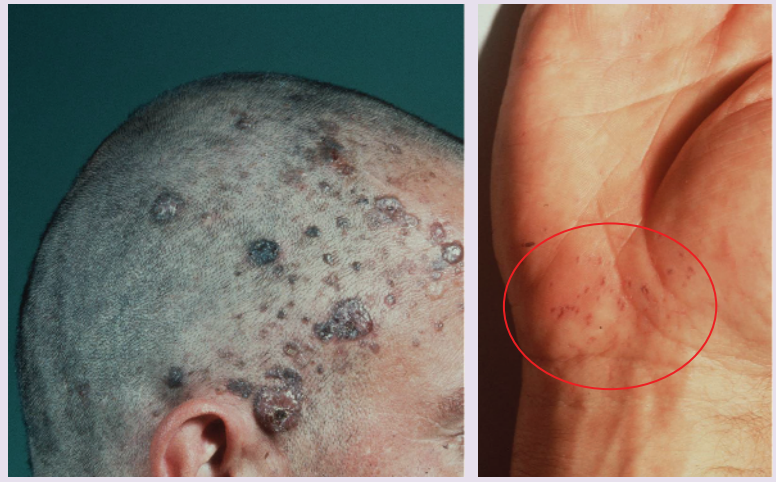
BASAL CELL CARCINOMA

Variant: Metatypic BCC with Squamoid Differentiation



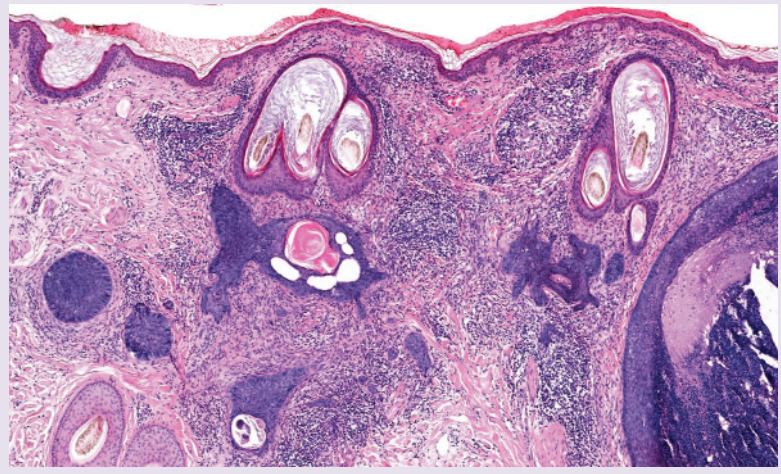
Hi: Cytological features indeterminate between classic basal cell carcinoma and squamous cell carcinoma. Often with typical basaloid tumor formation blending into squamous cell carcinoma-like zones of differentiation.

Syndromatic BCC (Basal Cell Nevus Syndrome, Gorlin–Goltz)



Multiple BCCs on the scalp

Palmar pits (circle)



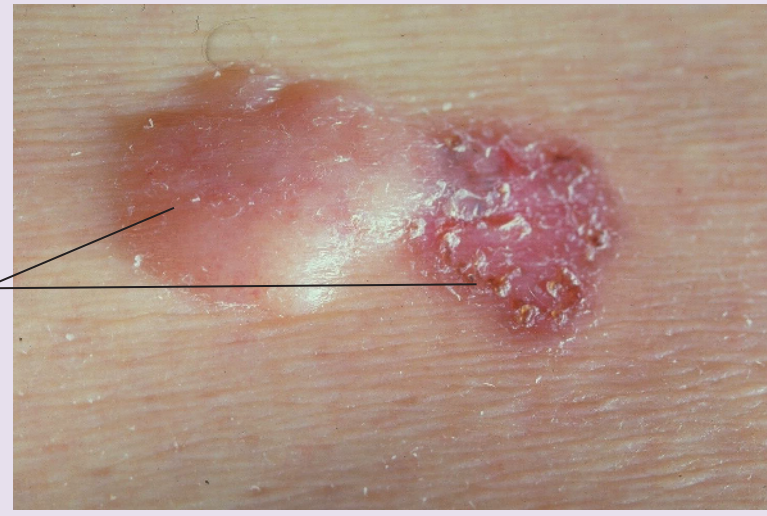
Proliferation of basaloid cells originating from infundibulocystic structures

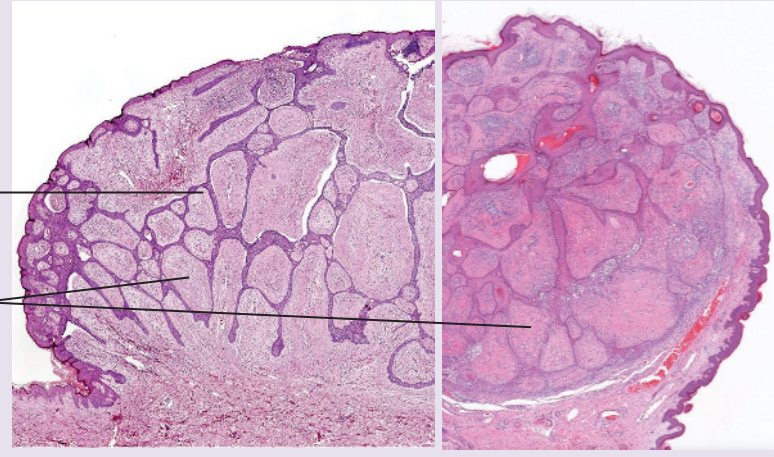
Several syndromes are associated with increased risk of BCC: Bazex–Dupré–Christol syndrome, Rombo syndrome, multiple hereditary infundibulocystic basal cell carcinomas, basaloid follicular hamartoma.

Cl: Autosomal dominant inherited mutation of the PTCH gene, which is responsible for disorders affecting the skin, skeleton, and central nervous system. Patients develop multiple basal cell carcinomas disseminated over trunk, face, and extremities. Initially, BCC may resemble small melanocytic nevi, before developing into larger BCCs. As in non-syndromatic BCCs, UV light and x-rays are promoting factors. Additional clinical signs include palmar pits (tiny defects of the stratum corneum), mandibular cysts, kyphoscoliosis, and calcified falx cerebri.

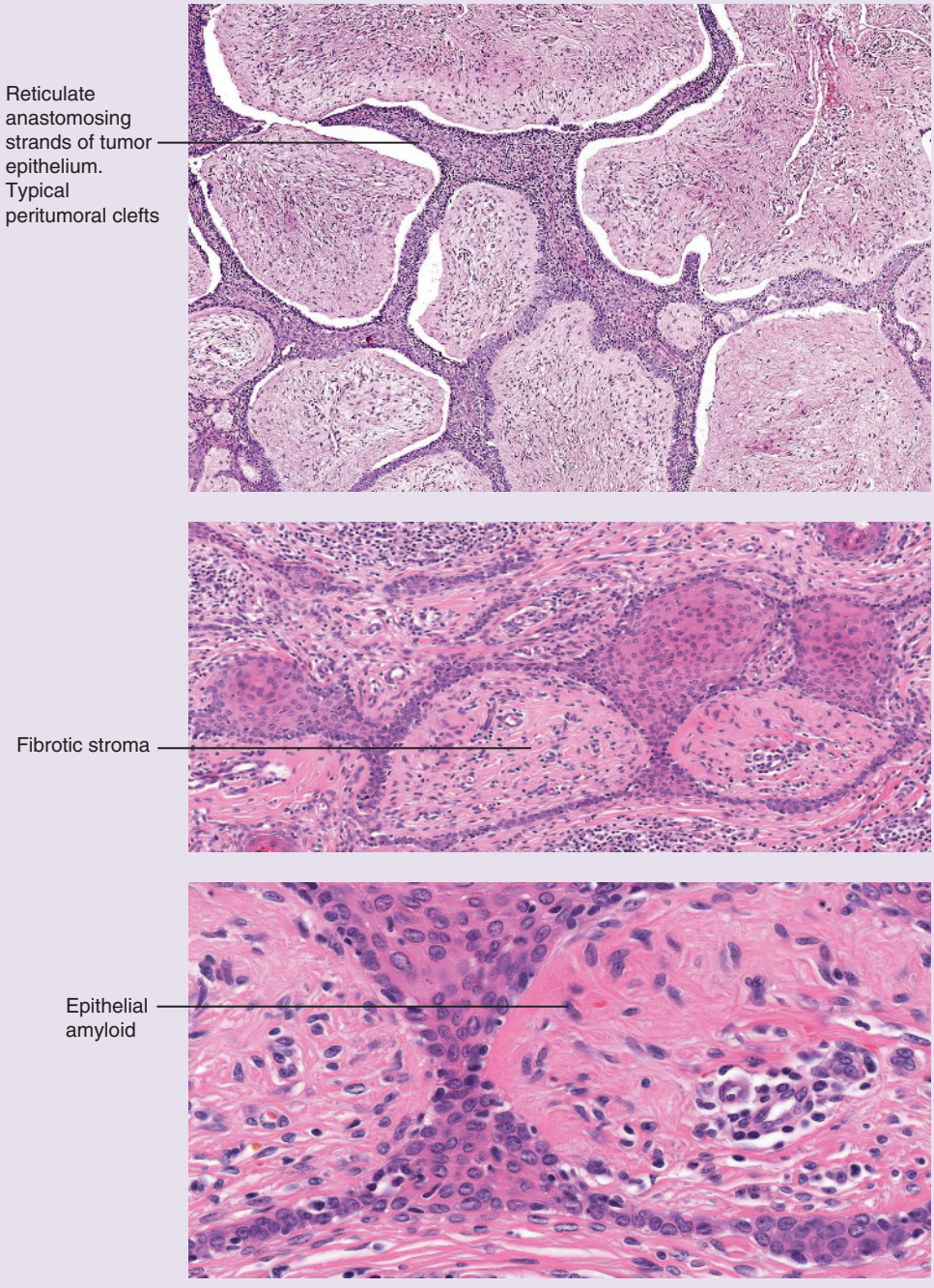
Hi: Corresponds to sporadic BCC. Most commonly nodular or superficial subtype. Early lesions may show an infundibulocystic origin.

Fibroepithelioma of Pinkus





Fibroepithelioma of Pinkus



Cl: Soft nodular, non-ulcerating lesion, preferentially in lumbosacral localisation.

Hi: Fibroepithelioma of Pinkus is considered to be a reticulated variant of BCC.

- Lacy strands of tumorous epithelium
- Connection with the epidermis
- Prominent fibromucinous stroma
- Peritumoral shrinkage clefts and peripheral palisading may be focally present
- At the tips of elongated tumor strands, there may be small, nub-like BerEP4-positive basaloid nests considered to be indicators of abortive hair bulb formation
- Focal positivity for PHLDA-1

SQUAMOUS CELL CARCINOMA

References

Bowen, A.R. and LeBoit, P.E. (2005) Fibroepithelioma of Pinkus is a fenestrated trichoblastoma. *Am J Dermatopathol* **27**(2): 149–54.

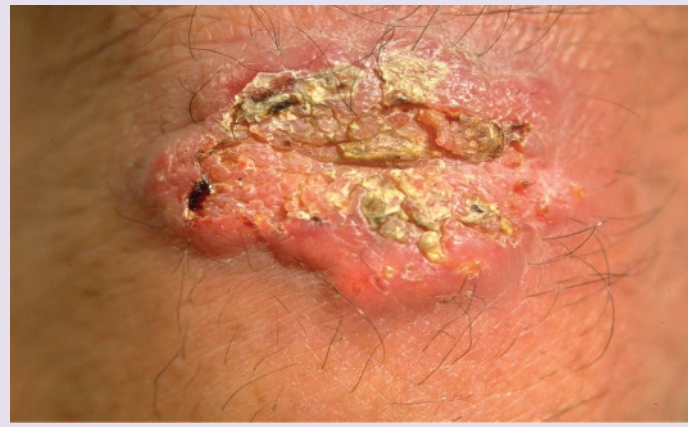
Katona, T.M., Ravis, S.M., Perkins, S.M., Moores, W.B., and Billings, S.D. (2007) Expression of androgen receptor by fibroepithelioma of Pinkus: evidence supporting classification as a basal cell carcinoma variant? *Am J Dermatopathol* **29**(1): 7–12.

Naeyaert, J.M., Pauwels, C., Geerts, M.L., and Verplancke, P. (2001) CD-34 and Ki-67 staining patterns of basaloid follicular hamartoma are different from those in fibroepithelioma of Pinkus and other variants of basal cell carcinoma. *J Cutan Pathol* **28**(10): 538–41.

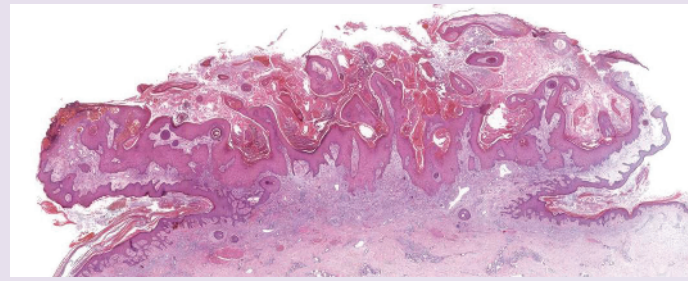
Stern, J.B., Haupt, H.M., and Smith, R.R. (1994) Fibroepithelioma of Pinkus. Eccrine duct spread of basal cell carcinoma. *Am J Dermatopathol* **16**(6): 585–7.

Squamous Cell Carcinoma (SCC)

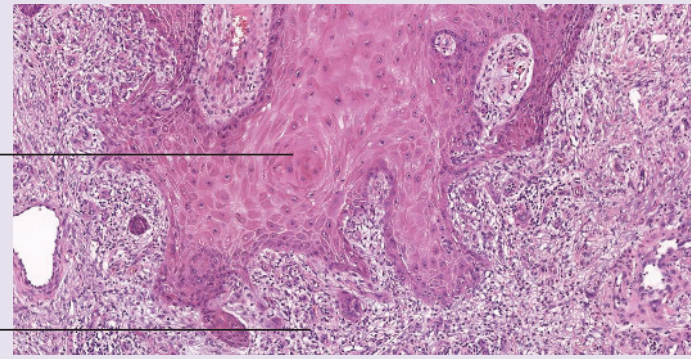
Variant: Well-Differentiated SCC



Tumor with hyperkeratotic crust



Exophytic proliferation of tumor cells

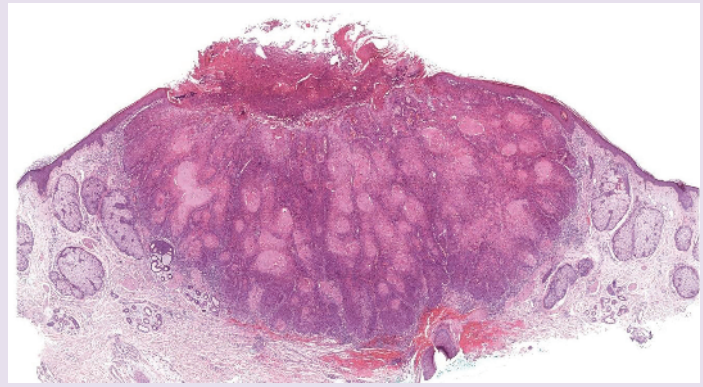


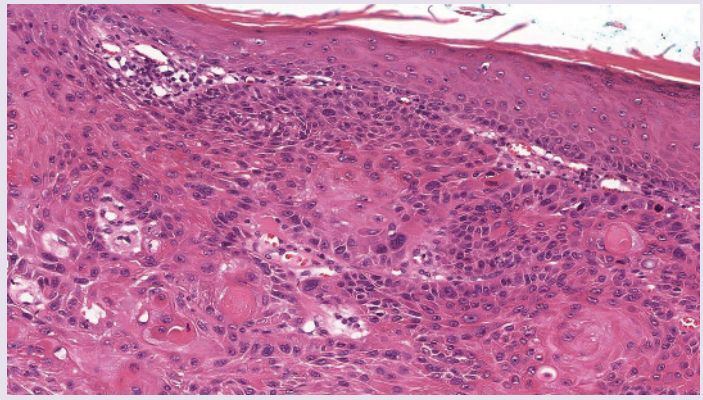
Pseudopod-like proliferation of atypical keratinocytes with islands of keratinization

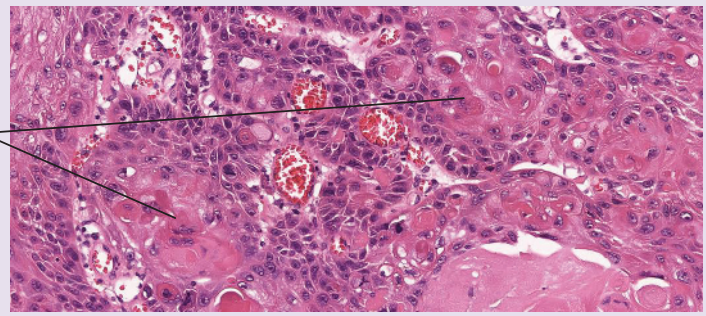
Tumor stroma with inflammatory infiltrate and fibrosis

SQUAMOUS CELL CARCINOMA

Variant: Well-Differentiated SCC







Cl: SCCs usually arise on chronically damaged skin (UV or ionizing irradiation, scars from wounds, burning, chronic ulcers, fistulae, lupus erythematosus, lupus vulgaris). They can appear anywhere on the body, including lips, tongue, and anogenital region. The lower third of the face, lower lip, earlobe, and dorsa of the hands are favored sites. The firm, nodular plaques are usually covered with hyperkeratotic crusts. Well-differentiated, highly keratinizing SCCs have an intermediate malignant potential with a low tendency to metastasize.

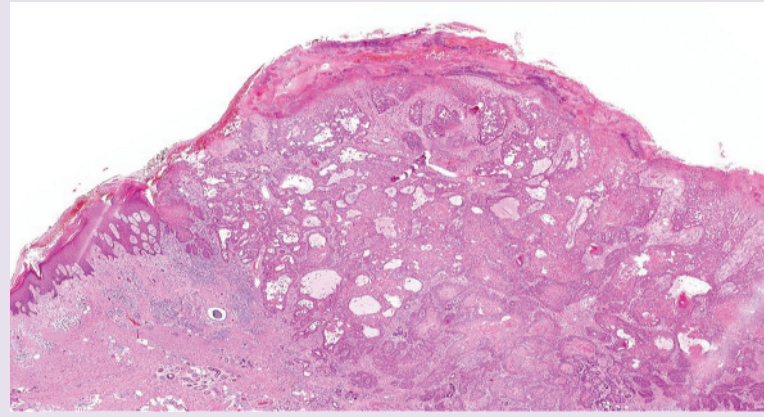
Hi:

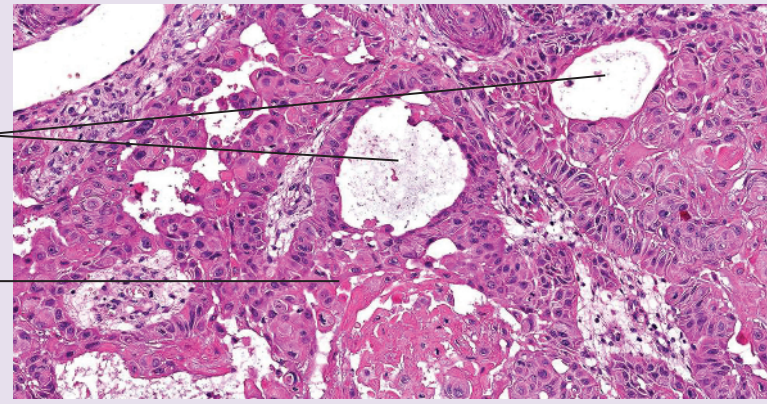
- Invasive epithelial tumor with asymmetry and poor circumscription
- Proliferation of pleomorphic epithelial tumor cells, corresponding to the keratinocytes of the spinous layer of the epidermis
- Eosinophilic cytoplasm

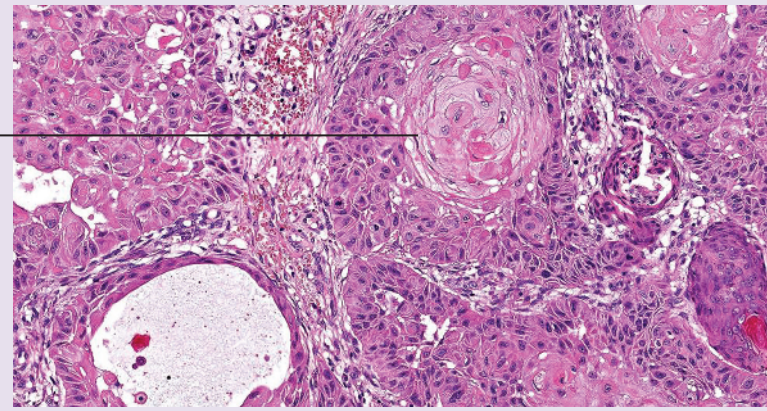
SQUAMOUS CELL CARCINOMA

- Intercellular bridges
- Focal keratinization and horn pearls
- Mitoses
- Focal necroses, not as pronounced as in keratoacanthoma
- Infiltrative growth
- Sometimes tumoral acantholysis may be present, simulating pattern of angiosarcoma

Variant: Acantholytic SCC (Epithelioma Spinocellulare Segregans of Delacretaz)

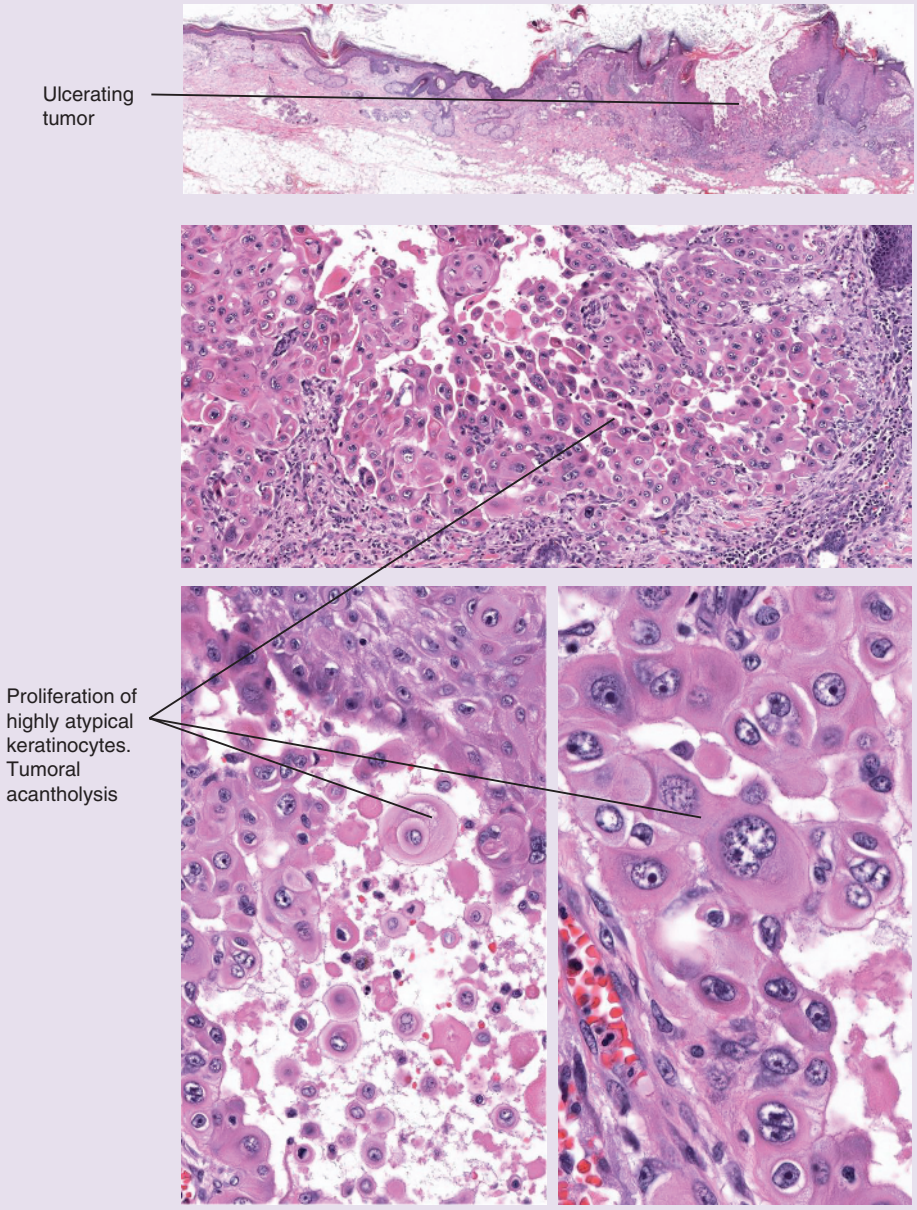






SQUAMOUS CELL CARCINOMA

Variant: Acantholytic SCC (Epithelioma Spinocellulare Segregans of Delacretaz)



This is not an entity in its own right but rather a poorly differentiated SCC variant with free-floating keratinocytes. Intercellular adhesion has been lost throughout the entire tumor, resulting in an angiosarcoma-like tumor pattern (tumoral acantholysis).
Cl: Minimal hyperkeratosis. Mostly ulcerated, bleeding or oozing, crust formation.

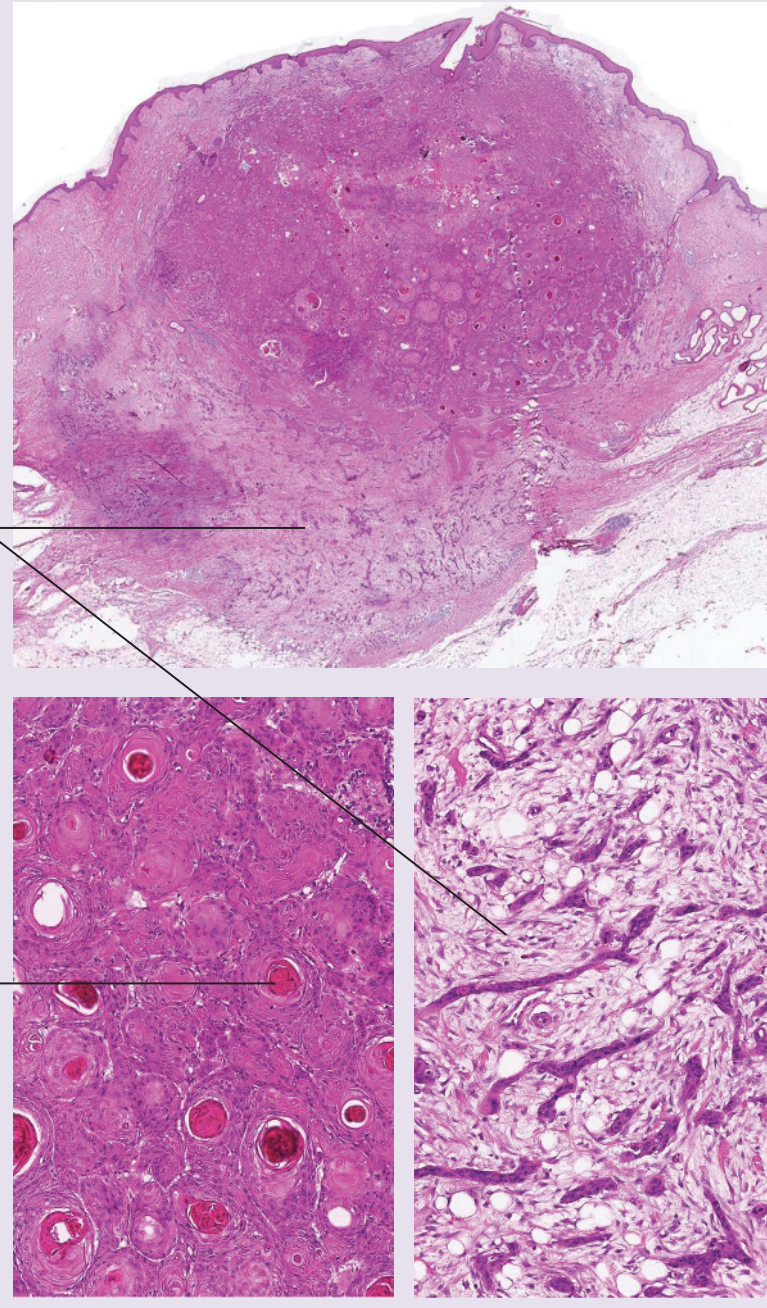
Hi:
- Pleomorphic and anaplastic keratinocytes
- Loss of intercellular bridges with acantholysis
- Inflammatory infiltrate, often containing many plasma cells

SQUAMOUS CELL CARCINOMA

Reference

Delacretaz, J., Madjedi, A.S., and Loretan, R.M. (1957) [Epithelioma spinocellulare segregans; the so-called adenoacanthoma of the sweat glands (Lever)]. *Hautarzt* **8**(11): 512–18.

Variant: Myxoid SCC



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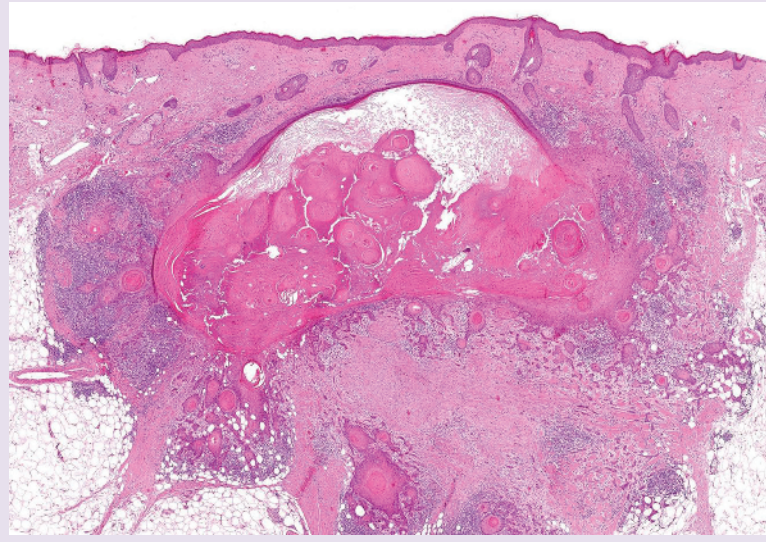
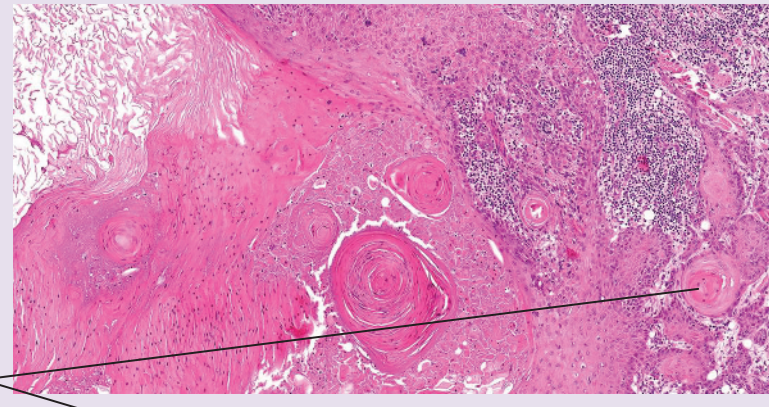
Cl: No specific clinical features.

Hi: Myxoid fibrous stroma.

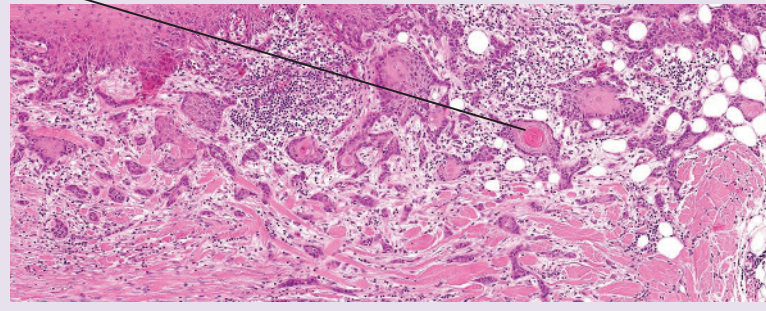
Variant: Follicular (Infundibular) SCC



Association with sebofollicular structures



Formation of pseudo-follicular structures

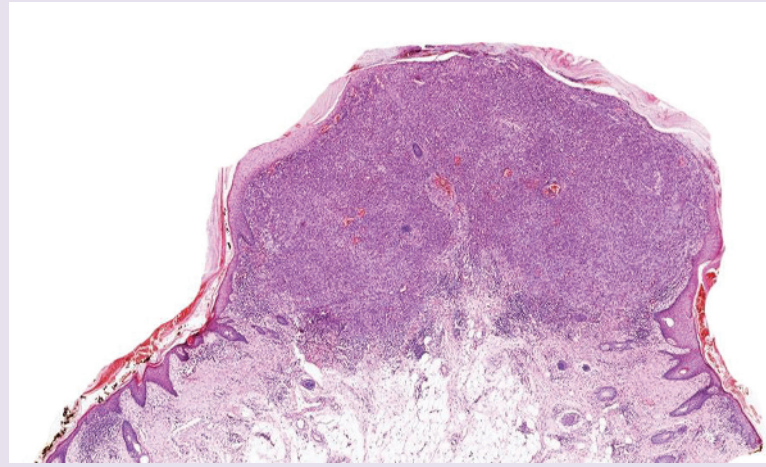


SQUAMOUS CELL CARCINOMA

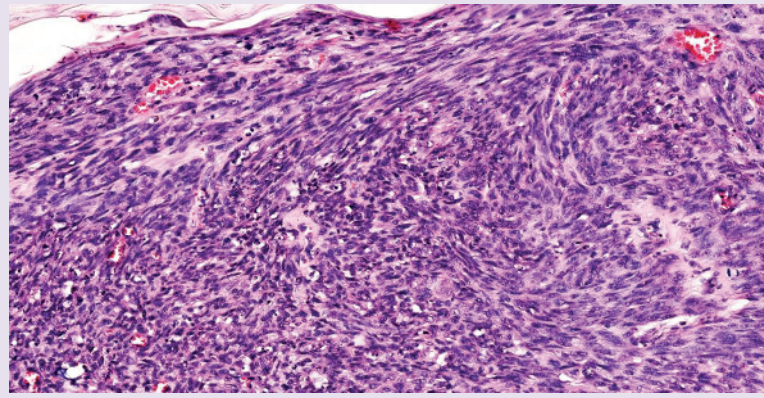
Some squamous cell carcinomas have follicular differentiation, arising from the infundibular portion of hair follicles. While they may overlap histologically with keratoacanthoma, clinically they are rarely confused with this entity.
Cl: Simulating keratoacanthoma.

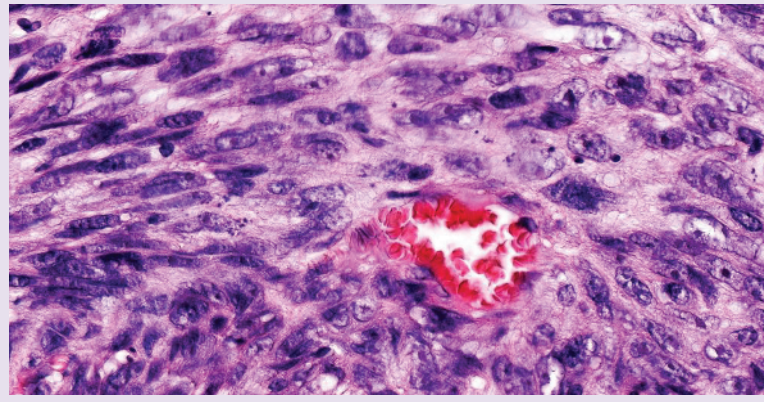
Hi:
- Arising from the infundibular portion of the hair follicle
- Abortive follicular structures

Variant: Spindle Cell (Fusicellular) SCC



Exophytic epithelial tumor without keratinization





Epithelial spindle cells

SQUAMOUS CELL CARCINOMA

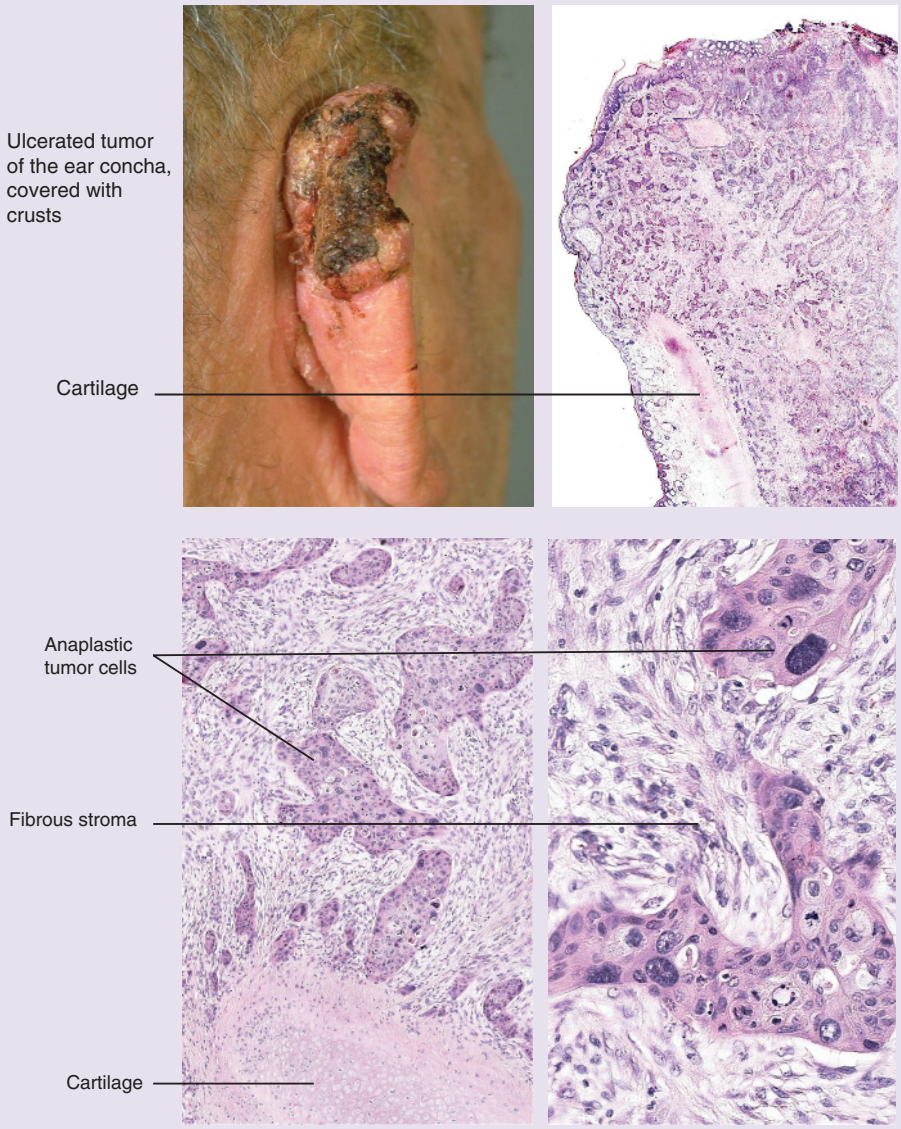
This variant presents with a tumor pattern that must be immunohistochemically separated from other epithelial and mesenchymal spindle cell tumors.
Cl: No specific clinical features.
Hi: Differentiation from other spindle cell tumors, especially from amelanotic melanoma, must be based on immunohistochemistry. Malignant melanoma reliably expresses S100 and SOX10, and is always negative for pancytokeratin. Spindled SCCs are frequently positive for vimentin, further adding to the confusion with mesenchymal neoplasms.

DD: Malignant (amelanotic) melanoma.

Squamous Cell Carcinomas in Special Sites

Cl: SCCs on ear, lip, penis, vulva, and tongue often are misdiagnosed at incipient stages of tumor evolution and may be mistaken for infectious disorders. However, due to the loss of differentiation, tumors at these sites often show a progressive course and tend to metastasize into the local lymph nodes.

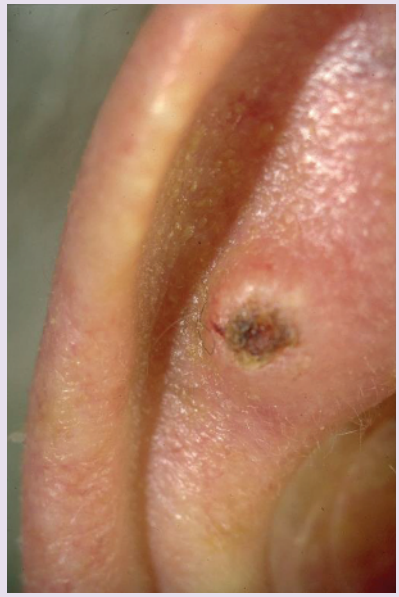
Squamous Cell Carcinomas in Special Sites



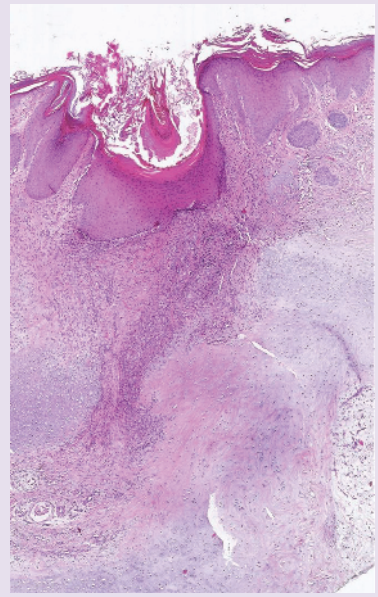
SQUAMOUS CELL CARCINOMA

Differential Diagnosis: Chondrodermatitis Nodularis Helicis of Winkler

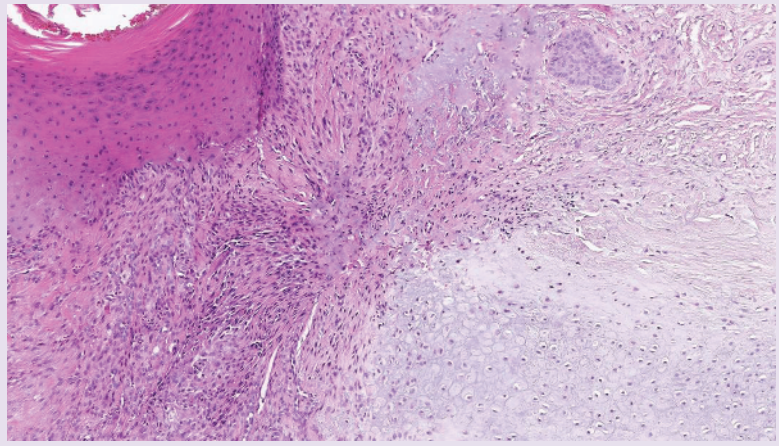
Crateriform lesion (left)



Endophytic crater with epidermal hyperplasia and adjacent granulation tissue, overlying eroded cartilage (right)

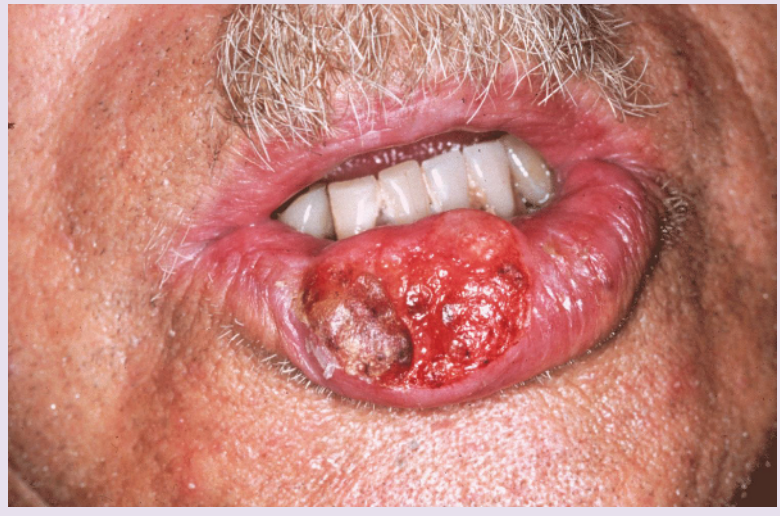


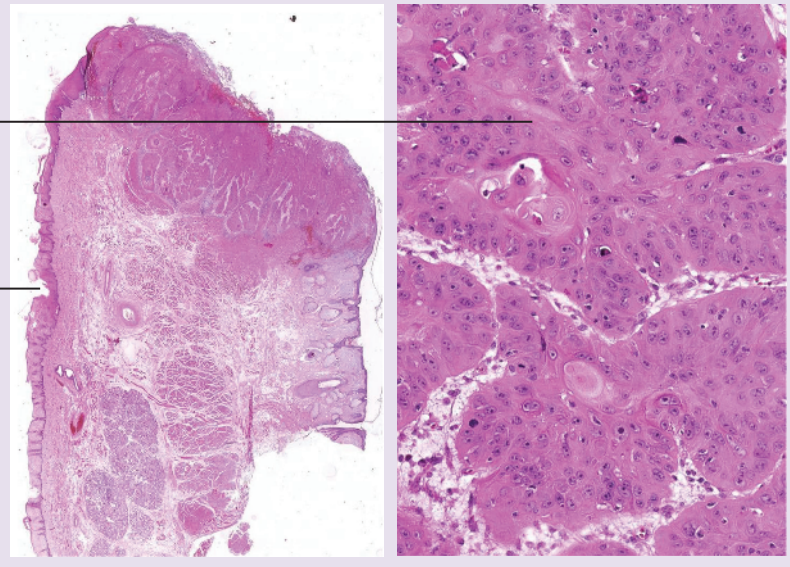
Epidermal hyperplasia, granulation tissue, eroded cartilage



SQUAMOUS CELL CARCINOMA

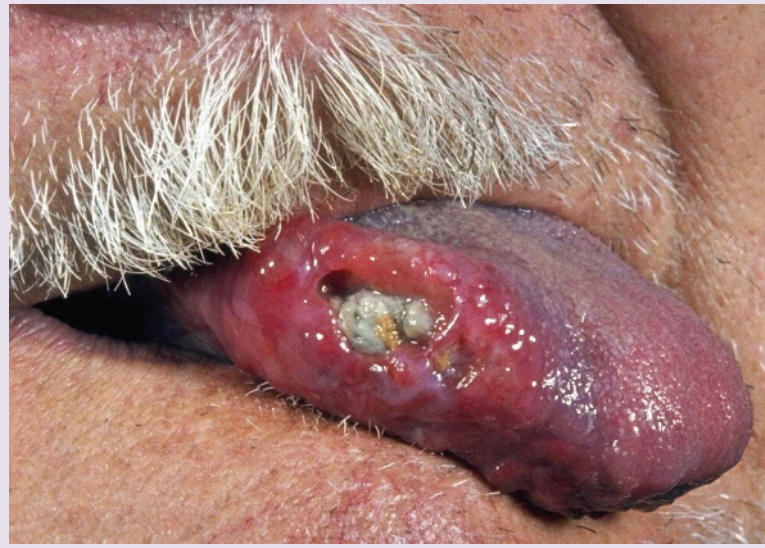
Special Sites: SCC of the Lip



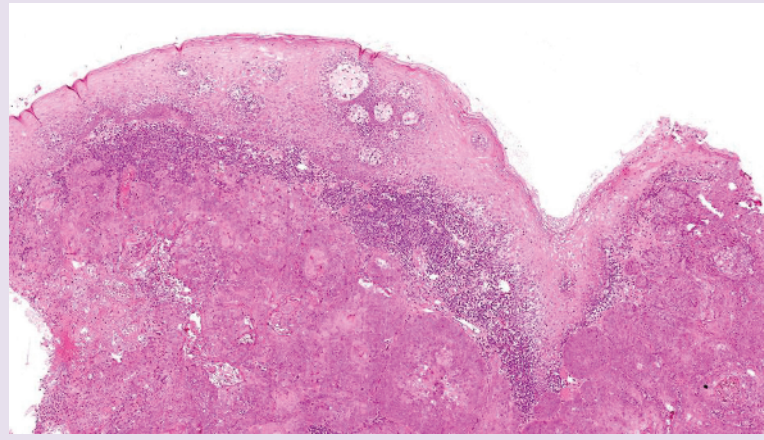


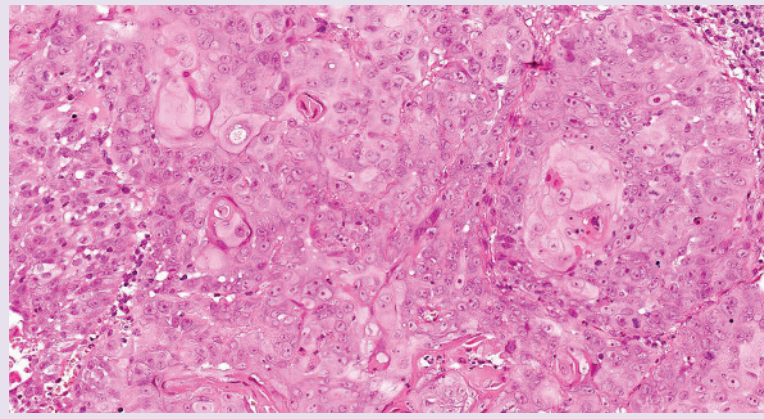
SQUAMOUS CELL CARCINOMA

Special Sites: SCC of the Tongue



Ulcerated SCC of the tongue



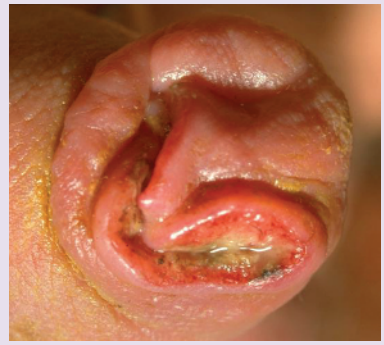


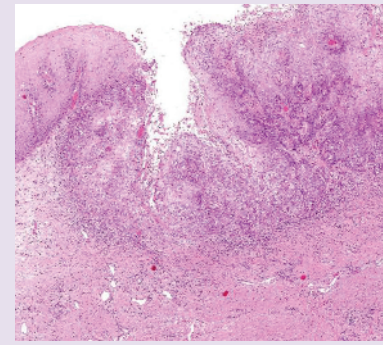
Invasive carcinoma with large, poorly differentiated squamous epithelial cells

SQUAMOUS CELL CARCINOMA

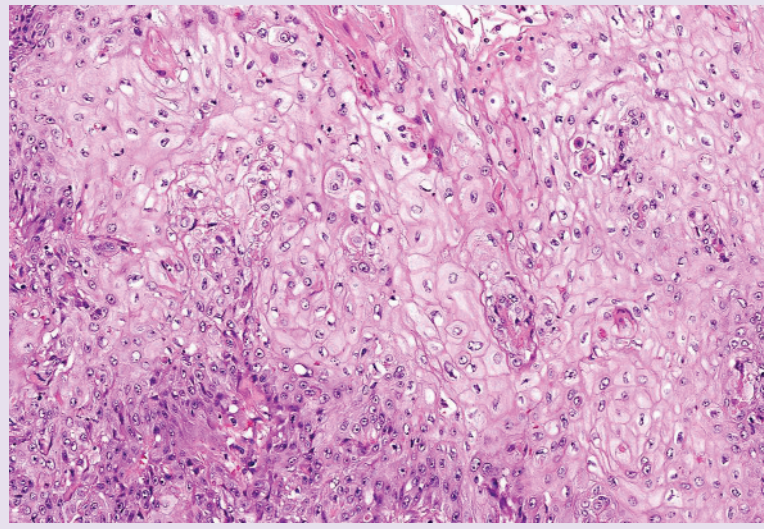
Special Sites: SCC of the Penis

Ulcerated tumor of the glans penis





Undifferentiated large, pale tumor cells



Hi:
- Often ulcerated
- Undifferentiated cytomorphology with minimal keratinization
- Highly atypical, pale anaplastic epithelial tumor cells
- Many mitoses
- Inflammatory infiltrate, containing many plasma cells

DD (ear): Chondrodermatitis nodularis helicis of Winkler.