



American Society for
Clinical Pathology

1355

**Cutaneous Adnexal Neoplasms:
Classification And A Practical
Diagnostic Approach**

David S. Cassarino, MD, PhD, FASCP

WEEKEND OF PATHOLOGY

*AMERICAN SOCIETY FOR CLINICAL PATHOLOGY
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1355 Cutaneous Adnexal Neoplasms: Classification and a Practical Diagnostic Approach

Director:

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General pathologists and dermatopathologists encounter daunting challenges when diagnosing cutaneous adnexal neoplasms, not the least of which is the sheer volume and variety of entities. In addition, frequently overlapping histologic findings, as with apocrine and eccrine tumors, often make reliable distinction difficult. You are sure to benefit from Dr. Cassarino's insights and approaches to meeting these challenges.

This highly practical presentation will include:

- Insights about the classification and diagnosis of cutaneous adnexal neoplasms
- A practical approach to the diagnosis of adnexal tumors, including the differential diagnosis of difficult lesions
- Criteria for distinction of benign vs. malignant tumors

In addition, Dr. Cassarino will review the hypothesis that most adnexal tumors derive from the folliculosebaceous apocrine unit and how it provides a logical and coherent classification system for adnexal tumors.

The course will include an interactive presentation of several clinical cases featuring challenging adnexal tumors.

Following this course, you will be able to:

- Reliably classify and diagnose cutaneous adnexal neoplasms.
- List the appropriate differential diagnosis for difficult adnexal tumors.
- Apply accepted criteria for the distinction of benign and malignant adnexal tumors.

**ASCP COURSE 1355
CUTANEOUS ADNEXAL NEOPLASMS:
CLASSIFICATION AND A PRACTICAL DIAGNOSTIC
APPROACH**

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**Disclosure information:
No conflicts to disclose**

LECTURE OUTLINE

PART 1

- I. Overview of basis for classification of adnexal tumors
- II. Tumors of follicular differentiation
- III. Tumors of sebaceous differentiation

PART 2

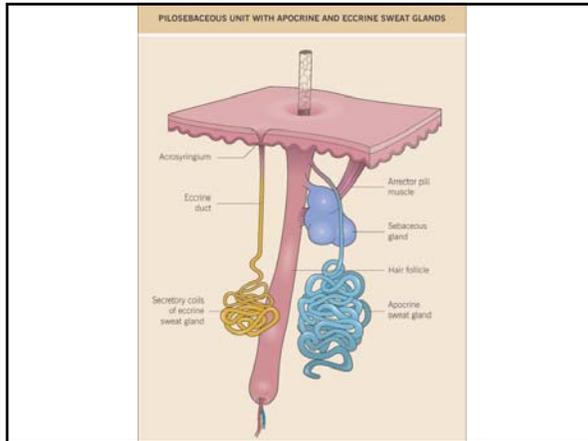
- IV. Tumors of apocrine differentiation
- V. Tumors of eccrine differentiation

**ARS QUESTIONS 1 - 2:
BACKGROUND**

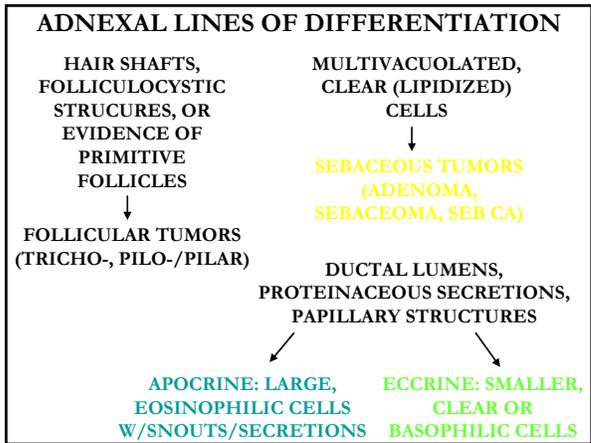
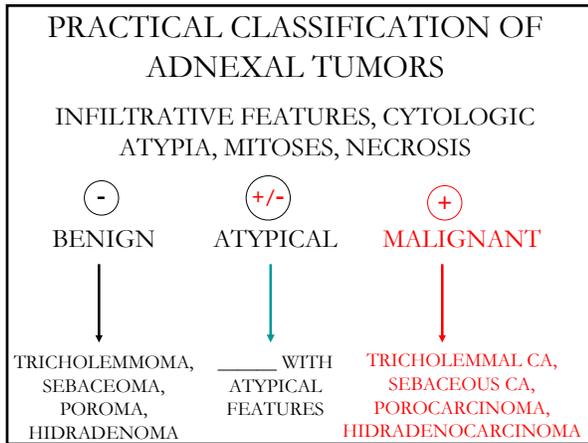
**I. BASIS FOR CLASSIFICATION
OF ADNEXAL TUMORS**

- Older classifications based on questionable morphologic and histochemical observations
 - Most of these are not specific for apocrine vs. eccrine diff nt
- Many tumors designated as eccrine or apocrine have features of the other category or features of adnexal ducts
 - Ducts of apocrine and eccrine nature show similar features and are essentially indistinguishable

- Histochemistry, immunohistochemistry, and even EM often give conflicting results
- Recent push to classify most "eccrine" tumors as "truly apocrine" (Ackerman school)
- Many tumors probably of follicular-sebaceous-apocrine unit (FSAU) derivation
 - Apocrine glands develop in assoc with follicular units, whereas eccrine glands develop separately



- Many follicular tumors can show focal sebaceous and/or apocrine differentiation
- Many ductal/glandular tumors may show focal follicular or sebaceous diff'nt
- Thus, if there are areas of follicular or sebaceous diff'nt in a ductal tumor, it is most likely apocrine -- not eccrine -- in nature
- Ultimately, not relevant for treatment or prognosis
- Benign versus malignant determination is crucial



- II. TUMORS OF FOLLICULAR & SEBACEOUS DIFFERENTIATION**
- A. TUMORS/HAMARTOMAS WITH FOLLICULAR DIFF'T:**
- Trichoadenoma
 - Trichofolliculoma
 - Trichoblastoma & trichoblastic carcinoma
 - Trichoepithelioma & desmoplastic trichoepithelioma
 - Pilomatricoma & pilomatrical carcinoma
 - Pilar sheath acanthoma
 - Proliferating pilar tumor (PPT) & malignant PPT

- Tricholemmoma, desmoplastic tricholemmoma, & tricholemmal carcinoma
 - Inverted follicular keratosis
 - Tumor of the follicular infundibulum
- TUMORS/HAMARTOMAS WITH PARTIAL FOLLICULAR DIFF'NT:**
- Fibrofolliculoma
 - Trichodiscoma
 - Microcystic adnexal carcinoma (MAC)
 - Basal cell carcinoma (follicular stem cell origin?) = trichoblastic carcinoma?

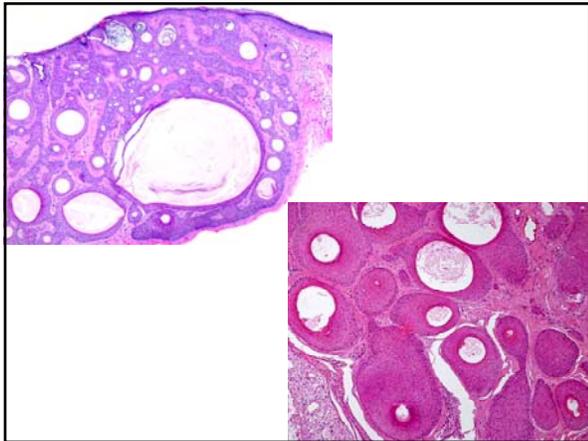
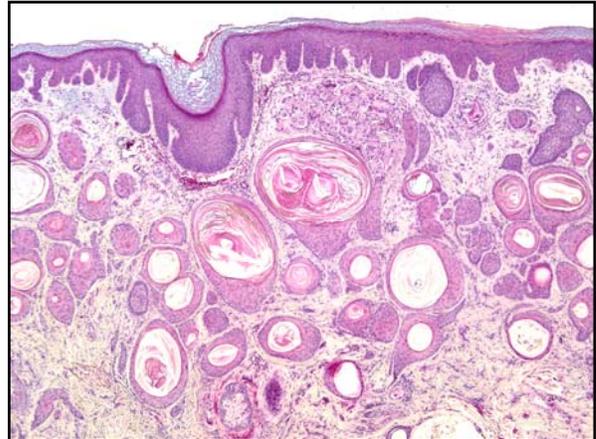
1. TRICHOADENOMA

Clinical:

- Rare, nodular lesion, usually presents on face or buttocks

Histology:

- Well-differentiated squamoid keratocysts dispersed within a fibrous stroma
- Cysts resemble infundibular portion of hair follicle, and are composed of stratified squamous lining with epidermoid keratinization
- Rare or no hair shafts present



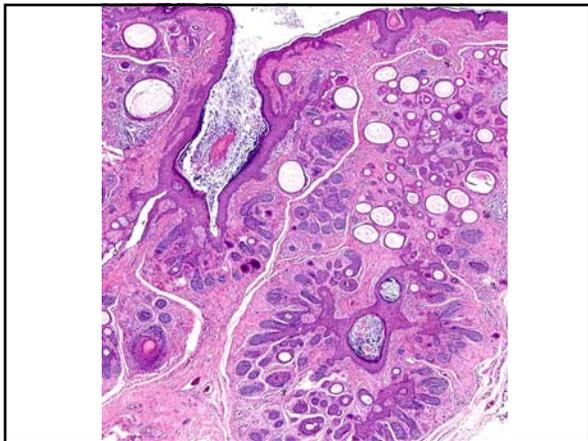
2. TRICHOFOLLICULOMA

Clinical:

- Typically occurs on face or scalp of adults as small, dome-shaped papule w/central punctum w/small hairs
- Same as, or closely related to, folliculosebaceous cystic hamartoma

Histology:

- Central, cystically dilated hair follicle from the wall of which arise many small, secondary small follicles; also see some keratinous debris and vellus hairs
- Scattered sebaceous diff'nt (rarely prominent)
- Surrounded by cellular fibrous stroma



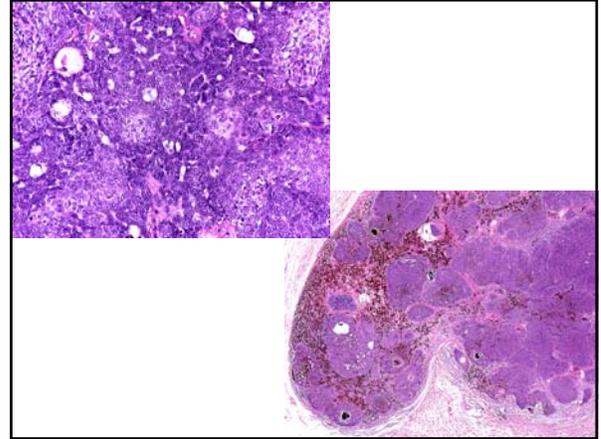
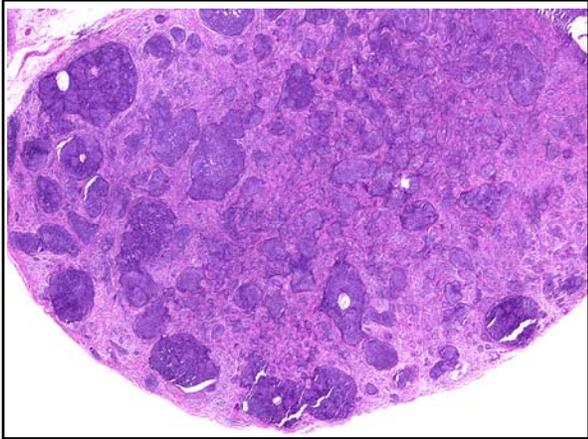
3. TRICHOBLASTOMA

Clinical:

- Rare benign tumor of hair germ
- Usually large tumors, > 1 cm, on the head esp. scalp, may be solitary or multiple

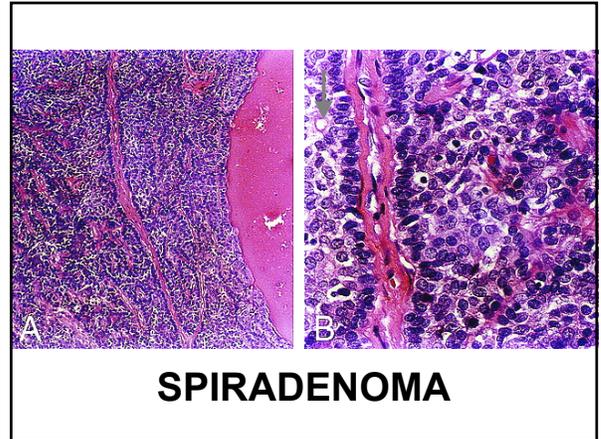
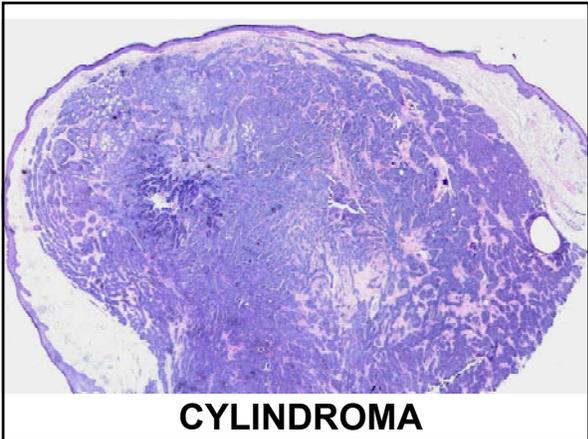
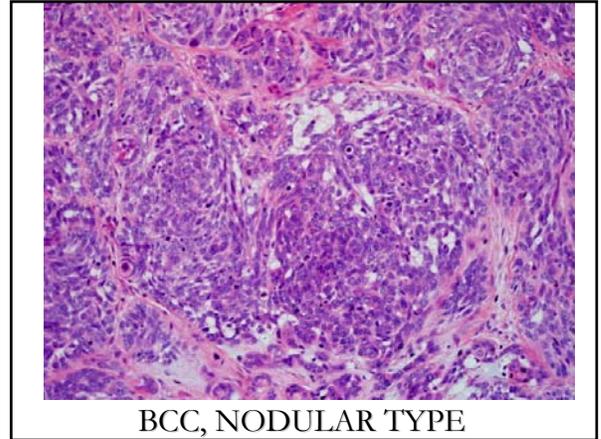
Histology:

- Large, circumscribed basaloid tumor w/out epidermal connections, located in mid to deep dermis w/subcutis extension
- Stromal induction with formation of primitive hair bulbs
- Cells are basaloid, but lack prominent peripheral palisading, mucoid stroma, mits and apoptoses, and show prominent pilar differentiation



TRICHOBLASTOMA: DIFFERENTIAL DIAGNOSIS

- BCC, NODULAR TYPE:**
 - Tumor-stroma retraction artifact, mucinous stroma, prominent palisading, and mitoses and apoptoses are abundant
- DUCTAL TUMORS:**
 - **CYLINDROMA:** Dermal nodules composed of "jigsaw-puzzle"-like irregular nests of basaloid cells with ductal diff'nt
 - **SPIRADENOMA:** Dermal nodules-sheet like proliferation of basaloid and clear cells with ducts



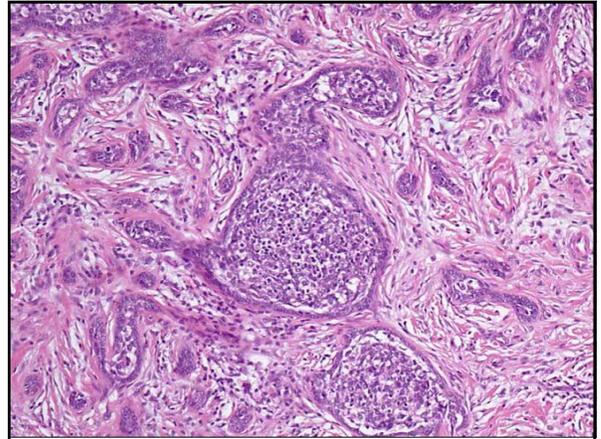
TRICHOBLASTOMA VARIANT: CUTANEOUS LYMPHADENOMA

Clinical:

- Considered a rare type of trichoblastoma
- Small nodule on face or legs, often present for yrs

Histology:

- Multiple lobules of basaloid cells within fibrous stroma
- May have peripheral pallisading, focal follicular or sebaceous diff'nt
- Intimately admixed small, bland lymphocytes



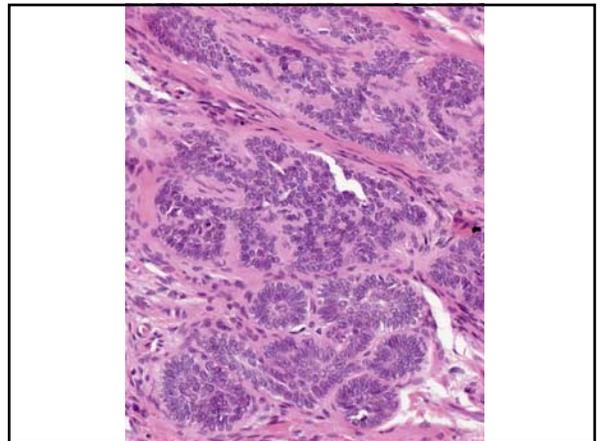
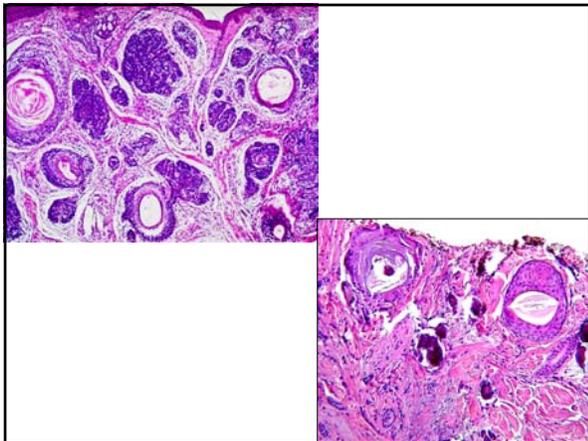
4. TRICHOEPITHELIOMA

Clinical:

- Tend to occur on the head and neck region of adults
- May be multiple lesions, usu. in children, AD and occas. a/w/cylindromas (Brook-Spiegler syndrome)

Histology:

- Usually well-circum lesion in upper dermis, lobules of bland basaloid cells with well-formed keratocysts, may see calcifications, cellular fibrotic stroma
- May show peripheral pallisading, but no retraction or myxoid stroma like BCC, and no/few mitoses and apoptotic bodies
- Superficial shave bx may not allow distinction from BCC



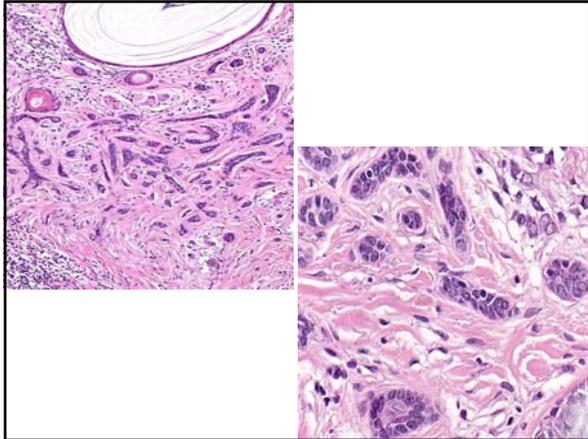
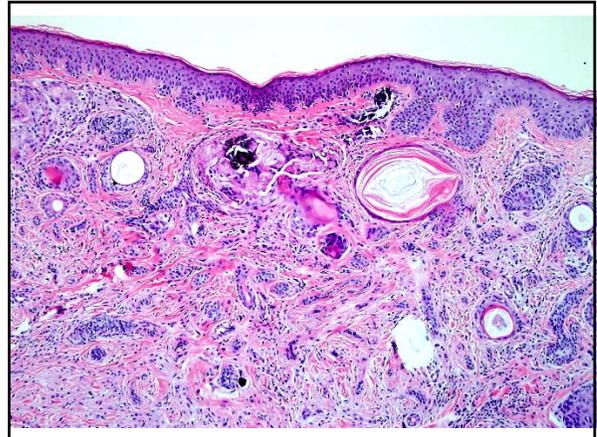
5. DESMOPLASTIC TRICHOEPITHELIOMA

Clinical:

- Head and neck, favors young adults, slow growing indurated plaque, may mimic a malignancy (usu. BCC)

Histology:

- Infiltrative-appearing cords and small nests, w/desmo-plastic stroma, occasional keratocysts, calcs, and granulomatous inflammation
- No deep infiltration or ductal diff'nt as in MAC, no perineural invasion
- Less cytologic atypia than sclerosing BCC, few mitoses or apoptotic bodies
- IPOX: +CKs, +BerEp4, -CK7, -EMA, -CEA, -Bcl-2, low Ki-67 (high in sBCC)



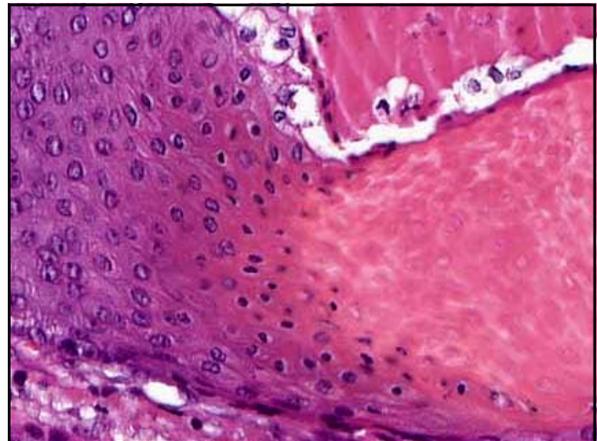
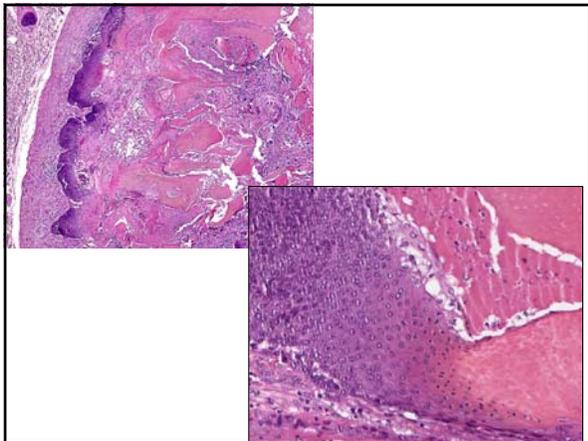
6. PILOMATRICOMA AND PILOMATRICAL CARCINOMA

Clinical:

- Slowly growing, solid nodule on head and neck of children/young adults
- Occasionally multiple, may be assoc. w/Turner's

Histology:

- Biphasic pop. of dark basaloid cells and pale eosinophil "ghost cells"
- May show brisk mitotic activity in basal cells
- Calcifications common, even bone formation may be seen



PILOMATRICAL CARCINOMA

Clinical:

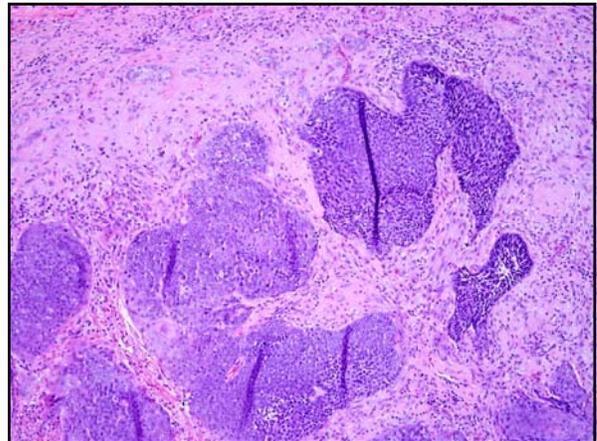
- Rare tumor, usually older males on upper back or neck, rapidly growing, may arise in pilomatricoma

Histology:

- Infiltrative nests and cords of hyperchromatic basophilic cells, with necrosis and high mitotic activity, occas. perineural invasion

Prognosis:

- High rates of recurrence and metastasis to lymph nodes and lung



7. PILAR SHEATH ACANTHOMA

Clinical:

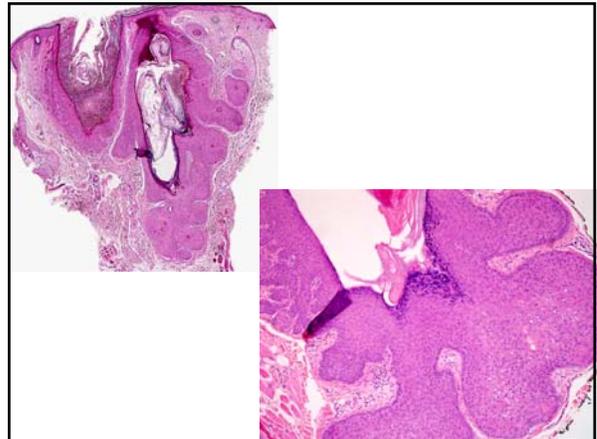
- Rare tumor, most almost exclusively on upper lip
- Usu. 0.5 – 1 cm, w/central pore plugged w/keratin

Histology:

- Multiloculated, dilated follicle-like structure lined by keratinizing squamous epithelium with vacuolization and peripheral pallisading, with a thickened, hyalinized basement membrane

- DDX:

- ▶ Dilated pore of Winer: more comedomal, large dilated follicle, less acanthosis, more pigmentation
- ▶ Trichofolliculoma: central sinus surrounded by radiating, small well-diff nt follicles



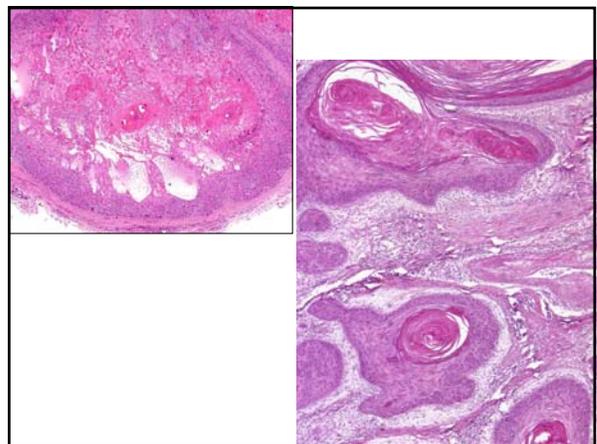
8. PROLIFERATING PILAR (TRICHOLEMAL) TUMOR/CYST (PPT) & MALIGNANT PPT

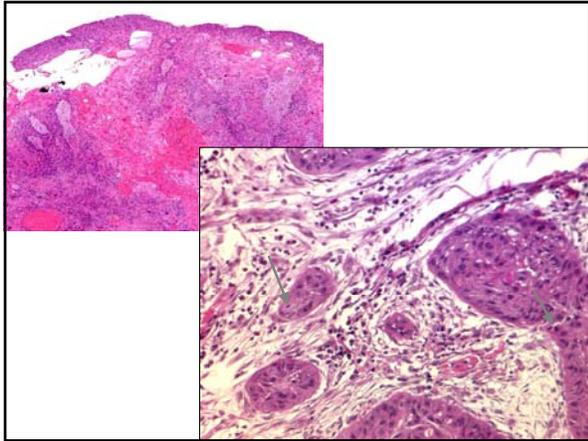
Clinical:

- Large, nodular, slow growing tumors on the scalp of mid- to older-aged pts, F > M
- High recurrence potential, but malignant PPT uncommon (despite Ackerman's characterization of all PPTs as malignant), but aggressive and arise in pre-existing PPT

Histology:

- Multilobulated, usu. well-circumscribed dermal tumor composed of mature squam cells with pilar keratinization
- Malignant PPT shows infiltrating SCC arising from PPT, with irregular tongues or solid sheets, high mitotic rate, necrosis





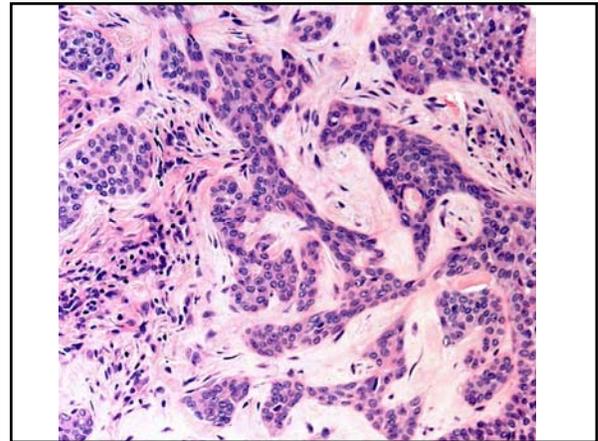
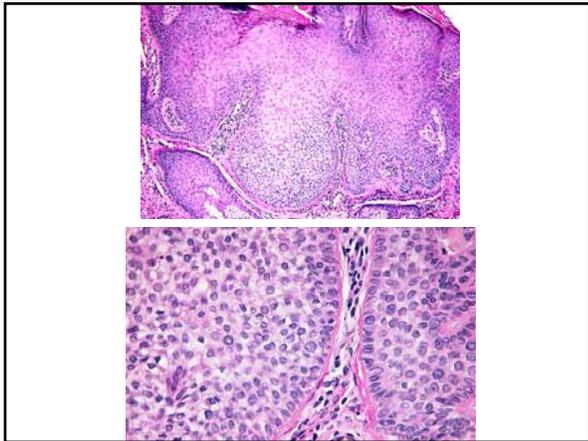
9. TRICHOLEMMOMA AND DESMOPLASTIC TRICHOLEMMOMA

Clinical:

- Small papular lesion(s) on face; if multiple, may be a/w/Cowden's syndrome; not a/w/HPV

Histology:

- Lobular, endophytic folliculocentric proliferation of pale to clear keratinocytes w/periph pallisading
- May have foci of keratinization, squamous eddies, and microcysts, usually thickened basement memb.
- Desmo TL: infiltrating cords in hyalinized stroma
- Cells are PAS+, diastase sensitive, may be CD34+



10. TRICHOLEMMAL CARCINOMA

Clinical:

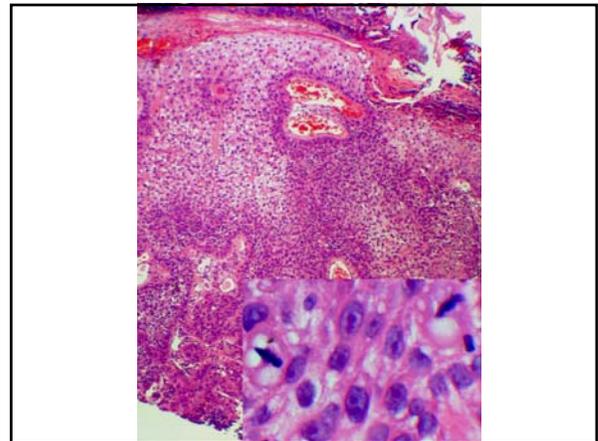
- Only rare cases reported, usu. sun-exposed skin of elderly patients, may be assoc. w/radiation exposure
- Clinical dx usu. BCC or SCC

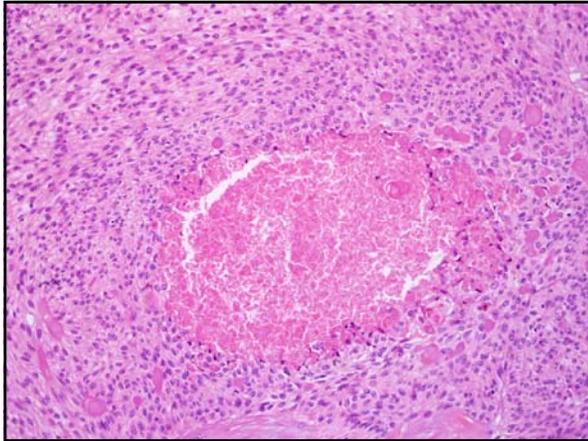
Histology:

- Multilobular, infiltrative proliferation of atypical, pale keratinocytes with peripheral palisading and hyalinized BM, shows a high mitotic rate
- Pagetoid spread may be present
- Diff nt dx: desmo TL, clear cell SCC, clear cell BCC, less likely: clear cell hidradenoma and metastatic RCC

Prognosis:

- Excellent, rare recurrences, no clearly documented metastases





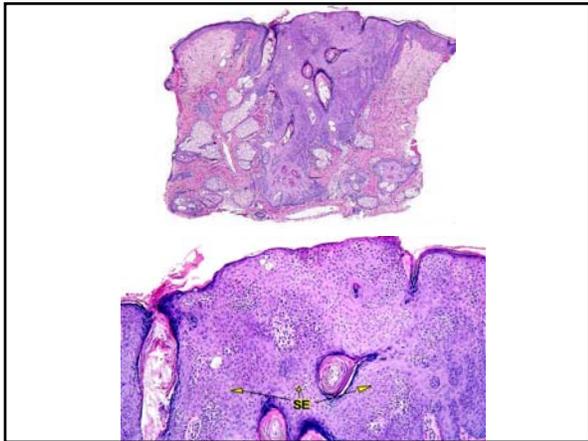
11. INVERTED FOLLICULAR KERATOSIS

Clinical:

- Solitary flesh-colored papule/nodule, head and neck - usu. cheeks and upper lip, M > F
- Probably not really a tumor, may be a variant of irritated seborrheic keratosis

Histology:

- Acanthotic, endophytic, squamoid proliferation w/numerous squamous eddies
- Several patterns:
 - ▶ Wart-like: exophytic with HK and PK
 - ▶ KA-like: exo-endophytic with lateral buttresses
 - ▶ Solid nodular form: endophytic, with cellular lobules
 - ▶ Uncommon cystic type: with clefts and small cysts



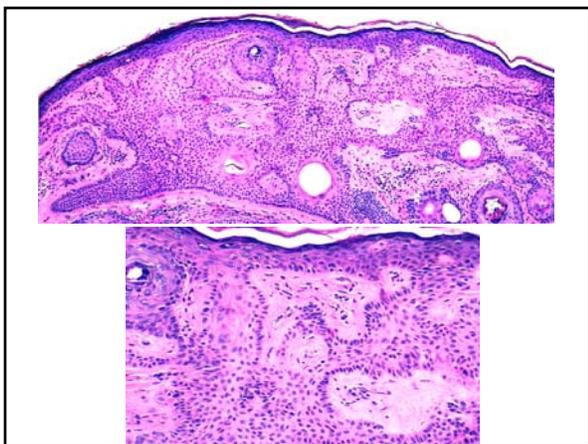
12. TUMOR OF THE FOLLICULAR INFUNDIBULUM

Clinical:

- Rare tumor, usu. solitary asymptomatic keratotic papule on head & neck or upper chest, may be a/w/Cowden's or nevus sebaceous
- Clinically, often diagnosed as basal cell carcinoma

Histology:

- Plate-like growth parallel to surface, composed of pale pink squamoid cells surrounded by peripheral palisade of basaloid cells
- Multiple connections w/epidermis, several follicles merge with underside of tumor, follicular bulbs and papillary mesenchymal bodies may be found



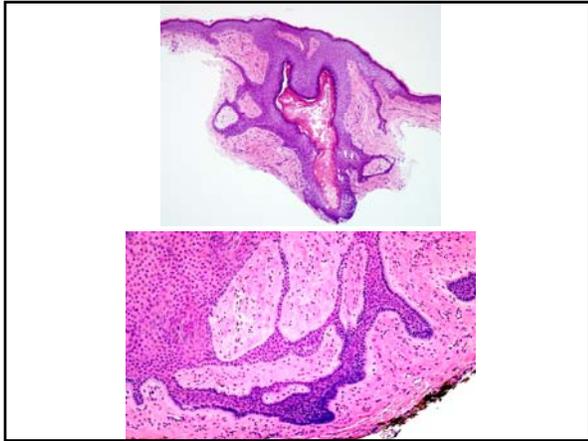
13. FIBROFOLLICULOMA

Clinical:

- Solitary or multiple small papule(s) on head & neck, trunk, arms, may see central follicle
- Multiple may be part of Birt-Hogg-Dube syndrome (AD, w/trichodiscomas, skin tags, renal Ca)
- Closely related to trichodiscomas, and may be same as mantleomas

Histology:

- Central hair w/dilated infundibulum and epithelial strands radiating from upper follicle
- Stroma shows loose fibrous tissue and mucin material
- Decrease in elastic fibers



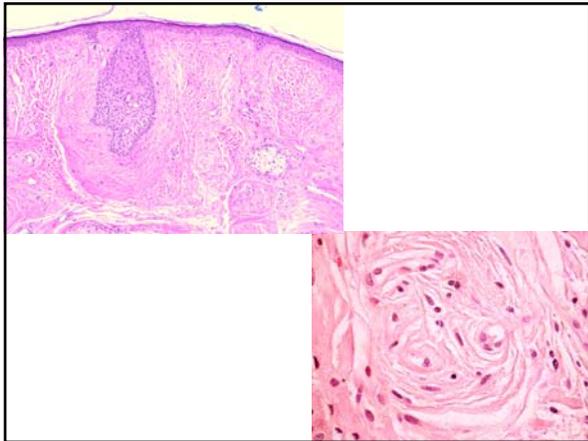
14. TRICHODISCOMA

Clinical:

- Asymptomatic, skin colored papules, usu. face, arms, trunk, w/hair follicle at edge
- May have numerous (even hundreds!) lesions, can be a/w/fibrofolliculomas and Birt-Hogg-Dube

Histology:

- Well demarcated, non-encapsulated, dome-shaped fibrovascular tumor composed of loose fibrillar stroma with mucin, ↓'d elastic fibers
- Hair follicle or folliculosebaceous collarette may be found at one margin



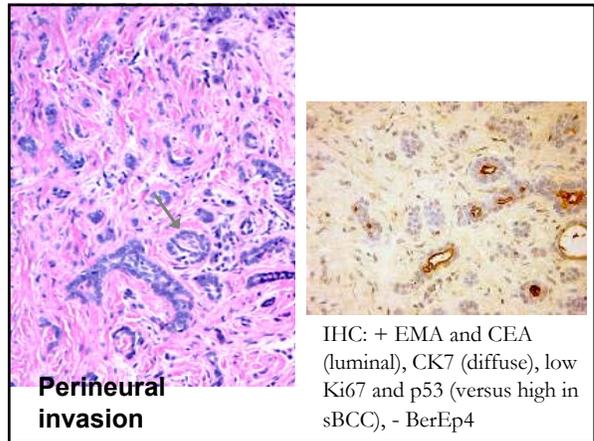
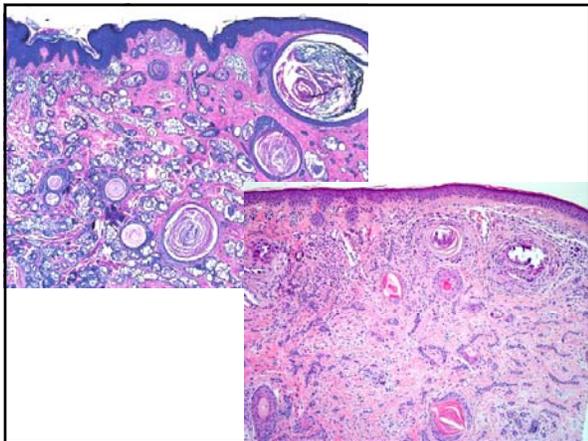
15. MICROCYSTIC ADNEXAL CARCINOMA (MAC)

Clinical:

- Occurs on face, usually lip and nasolabial area, followed by chin and cheeks, slowly enlarging firm plaque
- Locally aggressive tumor, high recurrence, but rare mets

Histology:

- Large, poorly circumscribed dermal tumor deeply infiltrating into subcutis (even muscle)
- Consists of bland adnexal (likely apocrine) cells forming cords and small ducts infiltrating desmoplastic stroma
- Superficial horn cysts and abortive follicles (FSAU-diffnt)
- Mitoses rare, perineural invasion frequent



Perineural invasion

IHC: + EMA and CEA (luminal), CK7 (diffuse), low Ki67 and p53 (versus high in sBCC), - BerEp4

• **Diff'nt diagnosis:**

1. **Infiltrative/sclerosing BCC:**

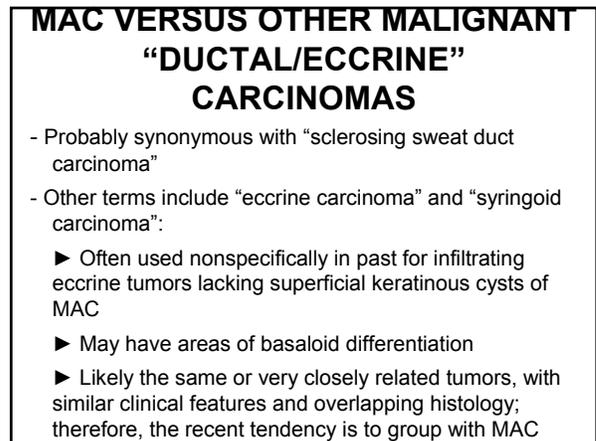
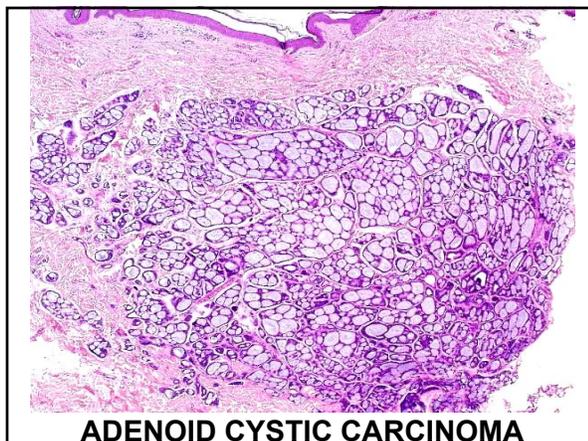
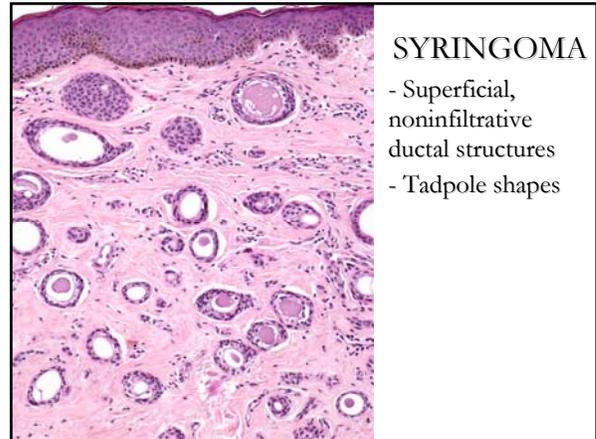
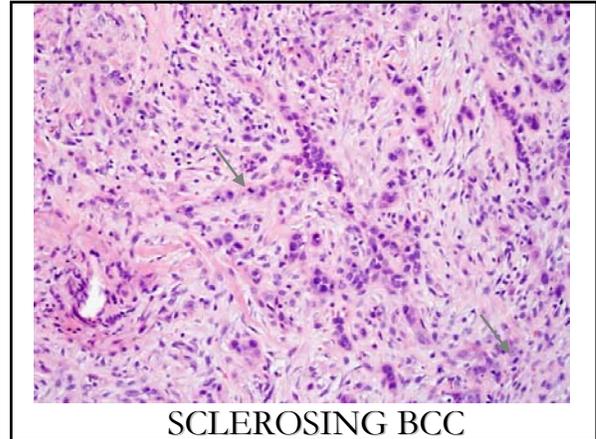
- Lacks superficial follicular cysts and ductal diff'nt, only rare perineural invas

2. **Desmoplastic trichoepithelioma:**

- Lacks deep invasion or perineural invasion, has calcifications, follicular but no ductal diff'nt

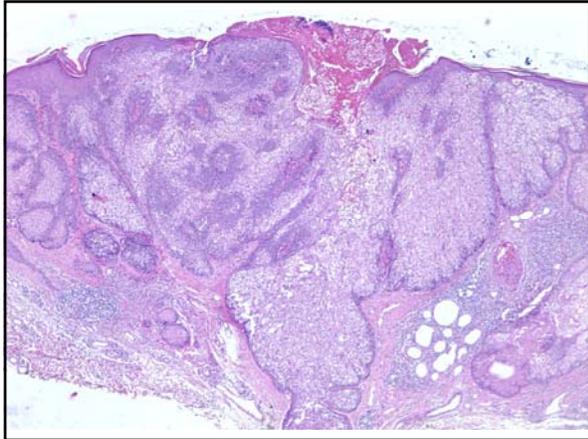
3. **Syringoma:**

- Bland ductal structures containing proteinaceous secretions (not keratin or hair material), lacks the deep infiltration, keratinocysts, and perineural invasion of MAC



III. CLASSIFICATION OF SEBACEOUS TUMORS

- Tumors of definite sebaceous differentiation:
 - Sebaceous adenoma
 - Sebaceoma ("sebaceous epithelioma"/basal cell carcinoma with sebaceous differentiation)
 - Sebaceous carcinoma
- Tumors of questionable/partial sebaceous differentiation:
 - Superficial epithelioma with sebaceous diff'nt
 - Mantleoma (may be fibrofolliculoma)



1. SEBACEOUS ADENOMA

Clinical:

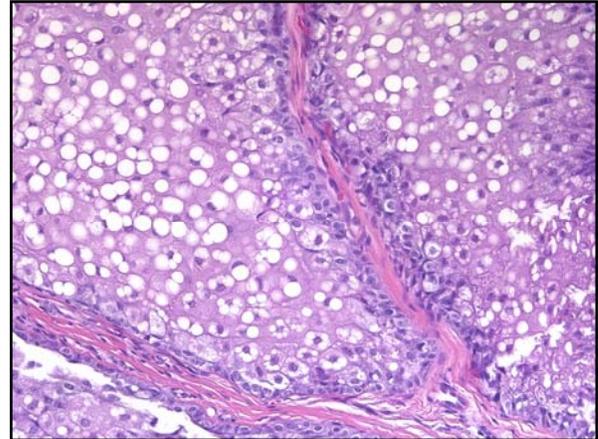
- Typically occur on face of elderly, eyelids very common
- May be associated with nevus sebaceous
- May be a/w/Muir-Torre Syndrome (MTS: auto dominant, microsatellite instability, a/w/internal malignancies, i.e., colon cancer), esp. multiple or cystic

Histology:

- Large, irregular lobules of mature-appearing sebocytes with peripheral rim of basaloid cells
- Lack of infiltration, cytologic atypia or mitoses

Prognosis:

- Excellent: small recurrence potential, zero metastatic



2. SEBACEOMA ("SEBACEOUS EPITHELIOMA")

Clinical:

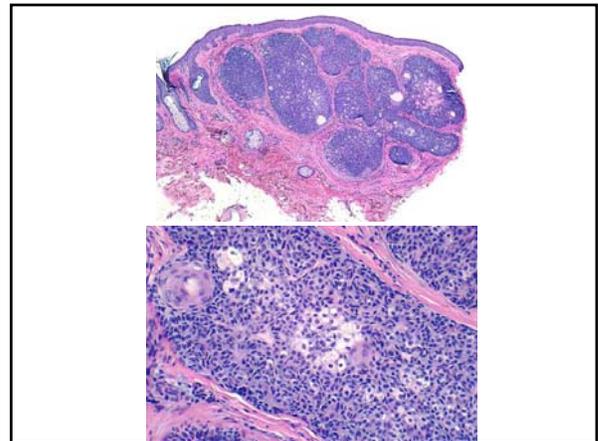
- Nodule on the face or scalp
- May be a/w/nevus sebaceous or Muir Torre Syndrome

Histology:

- Biphasic population: lobules and nests of basaloid cells, usually around periphery, with scattered (< 50%) sebaceous areas in center
- May have many mitotic figures, esp. in basaloid cells
- Overlap with BCC with sebaceous differentiation ("sebaceous epithelioma" – older term, no longer used)

Prognosis:

- Excellent: small recurrence potential, zero metastatic



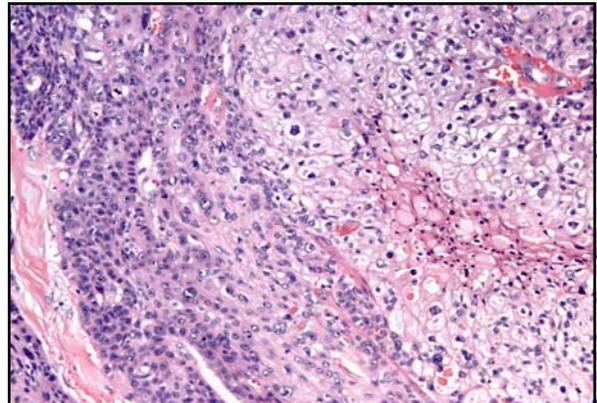
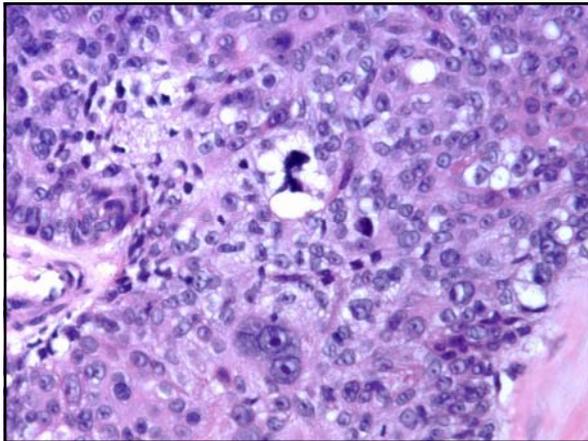
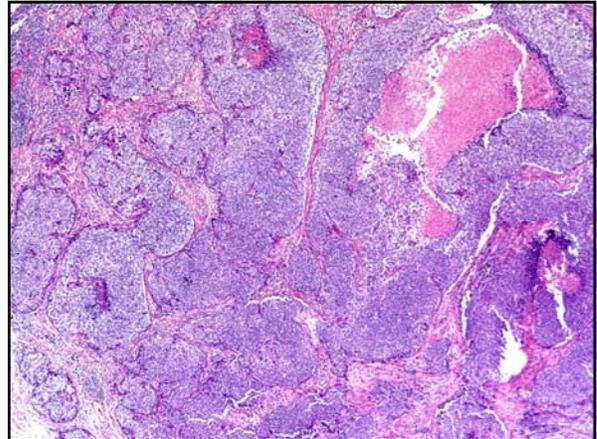
3. SEBACEOUS CARCINOMA

Clinical:

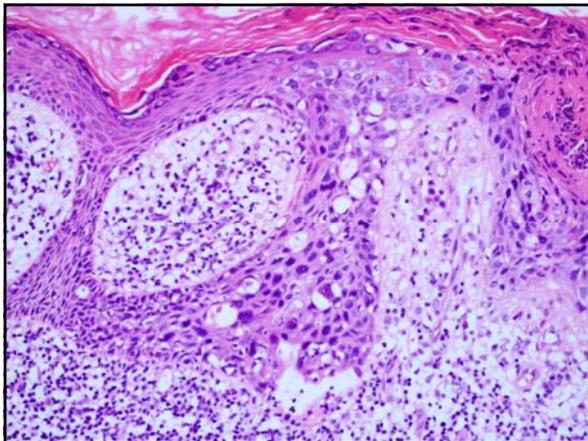
- Most on eyelids, followed by head and neck, presents as a nodule ± ulceration and hemorrhage
- Often misdiagnosed (>50% in some studies!), usually as BCC, SCC, Paget's, other adnexal tumors
- May also be a/w/Muir Torre Syndrome – less aggressive

Histology:

- Irregular, fusing lobules, nodules and sheet-like areas with infiltrative features
- Cytologic atypia, nuclear pleomorphism, multiple and atypical mitoses, often see areas of comedonecrosis
- IHC: EMA+, AR+, CD10±, CK7 ±, p53+, ↑ Ki-67, oil red O (frozens)



Juxtaposition of squamoid (left) and clear cell areas (right)



DIFFERENTIAL DIAGNOSIS:

1. Benign sebaceous tumors

- Sebaceous adenoma

Circumscribed growth of well-differentiated sebocytes surrounded by layer of small basaloid cells, > 50% well-differentiated sebocytes

- Sebaceoma

Circumscribed growth, < 50% well-differentiated sebocytes, > 50% bland basaloid cells; may see mitoses in basaloid cells, but lack atypia, mucinous stroma or retraction artifact

DISTINGUISHING SEBACEOUS TUMORS BY IHC

Sebaceous carcinomas show greater staining versus sebaceous adenomas for:

- p53 (50% versus 11%, $p < 0.05$) and
- Ki-67 (1.8+ versus 0.67+, $p < 0.05$)

➤ In addition, sebaceous carcinomas show reduced staining versus adenomas for:

- bcl-2 (7% versus 56%, $p < 0.05$) and
- p21 (16% versus 34%, $p < 0.05$)

➤ Sebaceomas and sebaceous hyperplasia show similar results to adenomas

DIFFERENTIAL DIAGNOSIS:

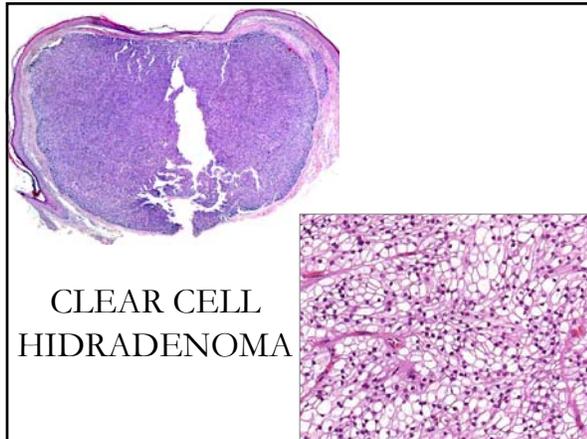
2. Other clear cell tumors

- Tricholemmal carcinoma

Peripheral palisading, uniformly clear cytoplasm lacking multivacuolar change, areas of squamoid diff, PAS+/PAS-D- (glycogen)

- Clear cell hidradenoma

Large nodular or cystic dermal-based lesion, usually lacks epidermal or follicular connections, lacks vacuoles, PAS+/PAS-D-; CEA & EMA highlight ductal structures



- Clear cell BCC:

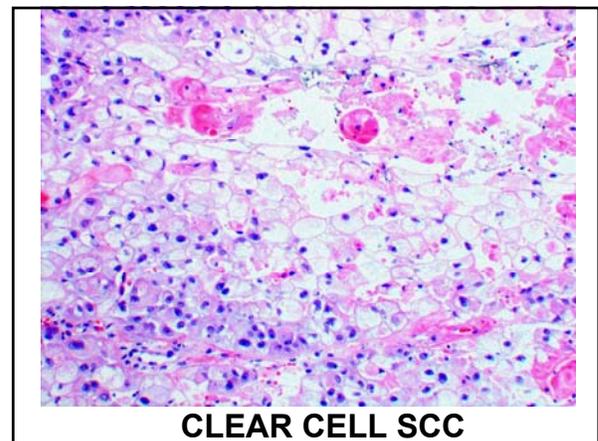
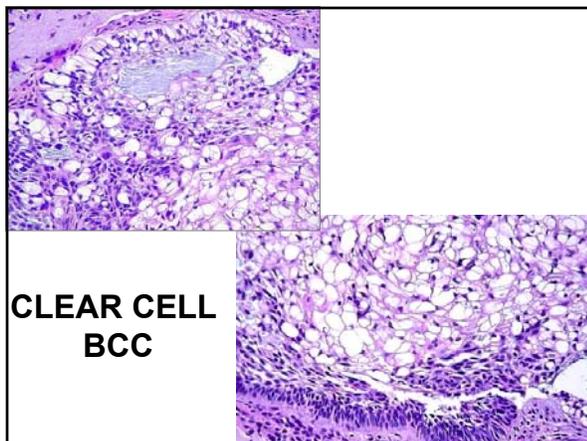
Rare variant, usually has areas of more typical BCC with palisading, retraction-artifact, mucinous stroma

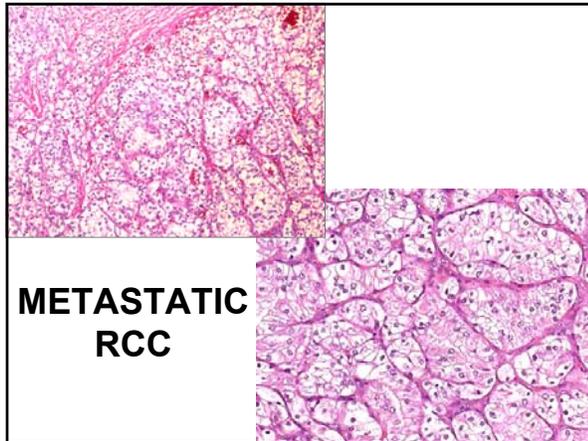
- Clear cell SCC/SCCis:

Should see areas of definite squamous diff'nt, often w/overlying SCC in situ (may be pagetoid); lack of cytoplasmic vacuoles and nuclear scalloping

- Metastatic renal cell carcinoma:

Usually well-circumscribed dermal nodule w/prominent vascularity; clear cells with often bland cytologic features; CK7-; CD10 & RCA+





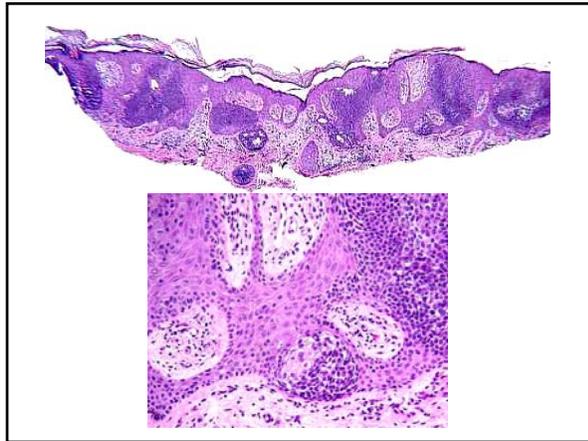
4. SUPERFICIAL EPITHELIOMA WITH SEBACEOUS DIFF'NT

Clinical:

- Rare tumor, mostly found on face of elderly
- Usually solitary, but may be multiple

Histology:

- Superficial, broad plate-like proliferation of small basaloid to squamoid (poroid) cells w/clusters of mature bland sebocytes
- Some resemblance to poroma with sebaceous diff'nt



LECTURE 2: APOCRINE AND ECCRINE TUMORS

IV. APOCRINE TUMORS

- Tumors of definite apocrine derivation:
 - Papillary tubular adenoma (Tubular apocrine adenoma)
 - Hidradenoma papilliferum
 - Syringocystadenoma papilliferum
 - Cutaneous mixed tumor (chondroid syringoma) and malignant mixed tumor
 - Apocrine (axillary) adenocarcinoma
- Tumors of modified apocrine glands:
 - Papillary adenoma of the nipple
 - Adenocarcinoma of Moll glands (eyelids)
 - Ceruminous carcinoma (extern auditory canal)
 - Paget's disease

IV. APOCRINE TUMORS

- Tumors of possible/occasional apocrine differentiation
 - Cylindroma and cylindromatous carcinoma
 - Adenoid cystic carcinoma
 - Aggressive digital adenocarcinoma
 - Primary cutaneous mucinous carcinoma and endocrine mucin-producing sweat gland carcinoma
 - Papillary "eccrine" adenoma
 - "Apocrine" poroma and porocarcinoma
 - "Apocrine" hidradenoma and hidradenocarcinoma

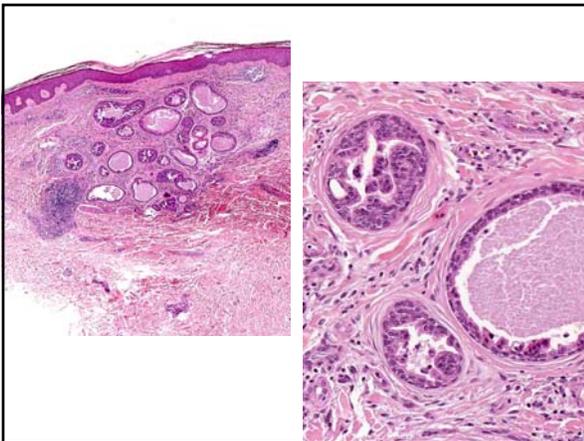
1. PAPILLARY TUBULAR ADENOMA (TUBULAR APOCRINE ADENOMA)

Clinical:

- Usually large, slow growing nodular tumor, with predilection for scalp
- Can also occur in axilla, cheek, and breast

Histology:

- Circumscribed lobules of bland tubular glands with 2-3 cell layers, the innermost of which shows papillary projections of apocrine cells with decapitation secretion
- May show overlap with syringocystadenoma papilliferum superficially



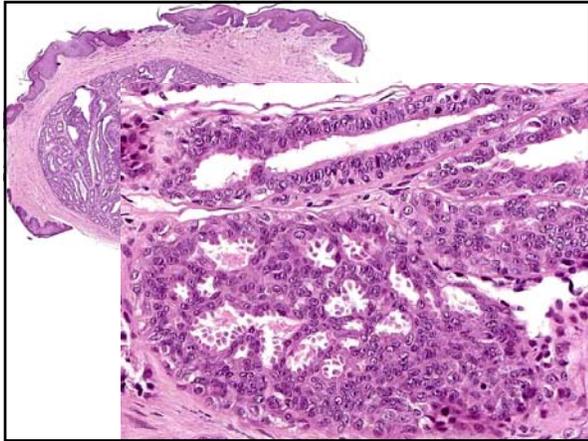
2. HIDRADENOMA PAPILLIFERUM

Clinical:

- Related to tubular apocrine adenoma, but occurs in genital and perianal area, rarely eyelid
- Usually presents as a solitary nodule, < 1 cm, in middle aged females

Histology:

- Well-circumscribed dermal nodule composed of arborizing trabeculae and glandular structures
- Thin layer of cells, which are tall columnar w/eosinophilic cytoplasm and luminal secretions



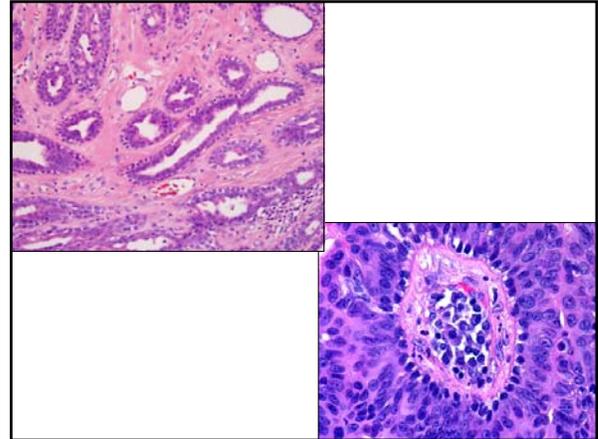
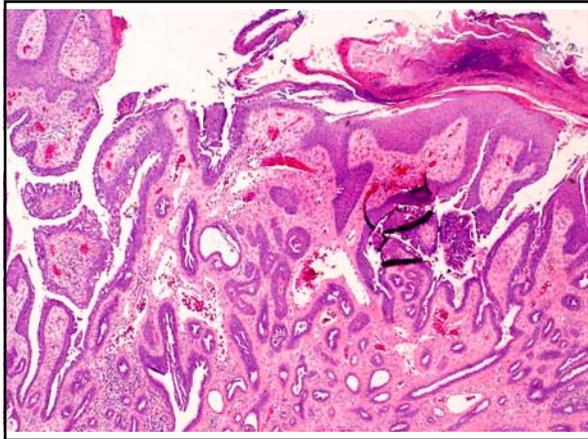
3. SYRINGOCYSTADENOMA PAPILLIFERUM

Clinical:

- Typically on scalp or forehead, followed by trunk, legs, eyelids, breast
- Raised verrucoid plaque or linear papules/nodules
- 1/2 present at birth, 1/3 assoc. w/**nevus sebaceous**

Histology:

- Invaginations of epidermis merge with ductal epithelium forming villous papillae and cystic areas
- Lined by 2 cell thick layer w/apocrine diff nt
- Stroma with prominent plasma cell infiltrate (IgA-related)



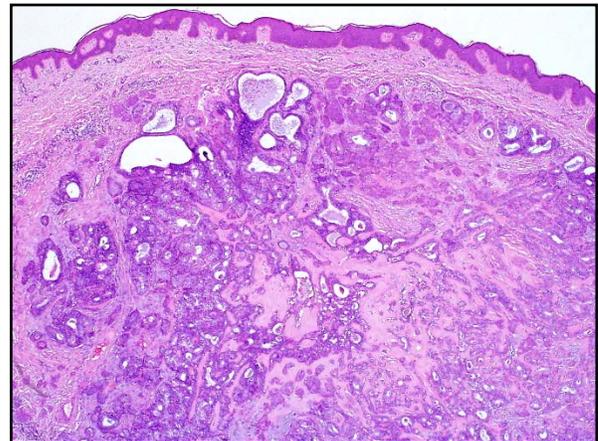
4. CUTANEOUS MIXED TUMOR (CHONDROID SYRINGOMA)

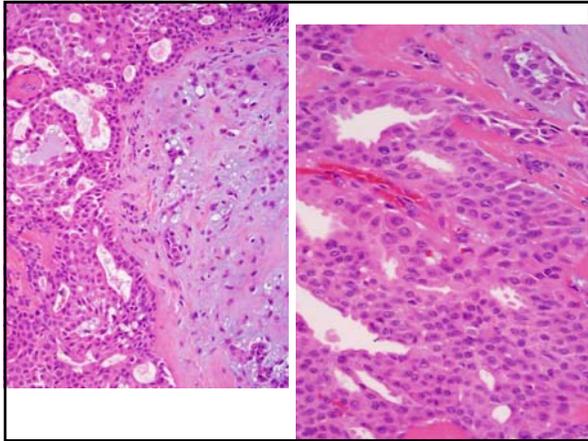
Clinical:

- Head and neck of middle to older aged
- Slowly growing papule/nodule, 0.5 – 3 cm.

Histology:

- Elongated tubules and glandular areas with occasional decapitation secretion, basal myoepithelial cells
- Myxoid to chondroid stroma, fibrous areas, may have cartilage or bone formation (myoepi-derived)
- Extremely rare malignant transformation





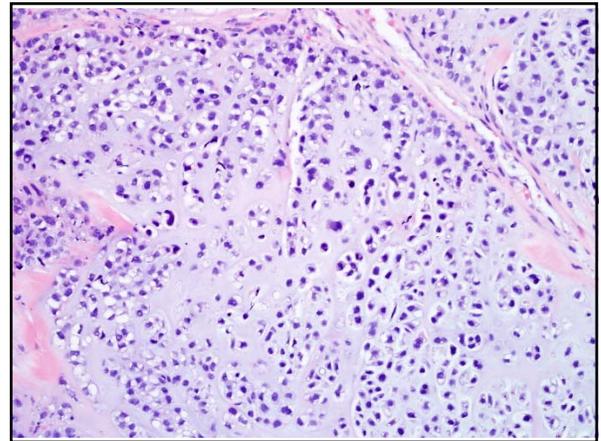
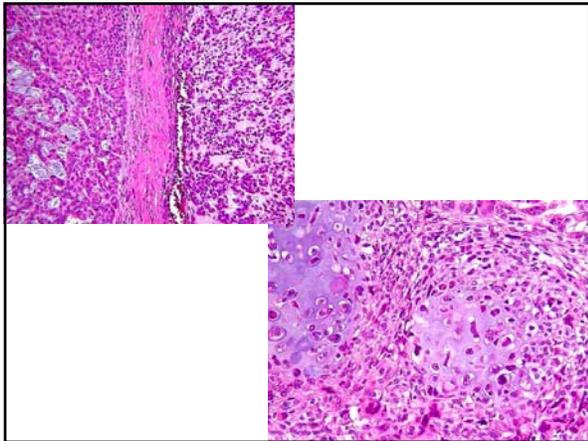
5. MALIGNANT MIXED TUMOR

Clinical:

- Usually on trunk and extremities (not head and neck like benign mixed tumor) of elderly
- Multilobulated appearance

Histology:

- Nests, chords, and sheet-like proliferation of atypical, epithelioid cells in a myxoid to chondroid stroma
- Distinguished from benign mixed tumor by infiltrative features, cellular pleomorphism, abundant mitoses, \pm necrosis



6. APOCRINE (AXILLARY) ADENOCARCINOMA

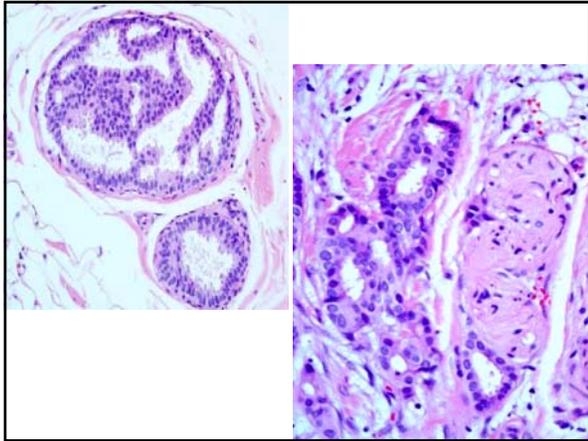
Clinical:

- Rare tumor, primarily axillary and anogenital, but occurs in other sites as well
- Presents as nodular/multinodular mass
- Lethal in up to 40% of cases

History:

- Unencapsulated tumor with variable patterns including papillary, tubular, and cord-like arrangements
- Infiltrative proliferation of apocrine cells w/low to high grade cytological atypia and mitoses





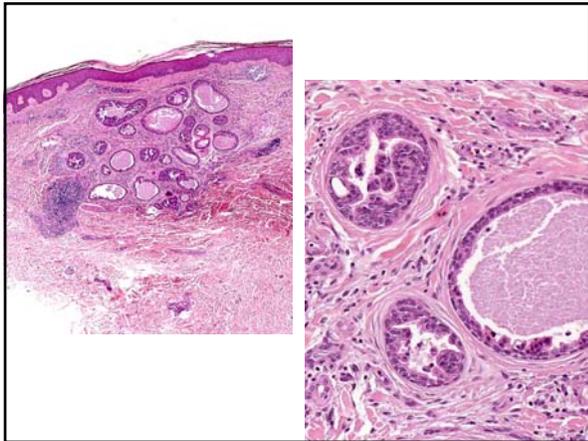
APOCRINE ADENOCARCINOMA

Differential Diagnosis:

1. **Apocrine tubular adenoma:** benign cytologic features and lack of infiltration or mitoses
2. **Metastatic adenocarcinoma, especially breast:** may be difficult without clinical history, exams

Immunohistochemistry:

- Most cases are strongly CK and GCDFGP +
- Often ER/PR positive – cannot distinguish from Breast CA
- Variable S100 and CEA staining



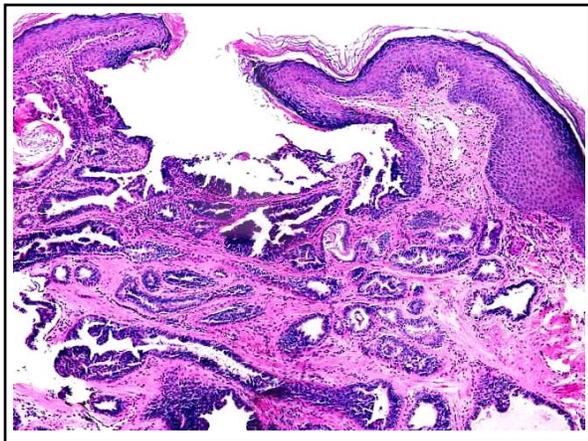
7. PAPILLARY ADENOMA OF THE NIPPLE (FLORID PAPILLOMATOSIS)

Clinical:

- Benign tumor which may mimic Paget's disease
- Rarely occurs in males

Histology:

- Well-circum, non-encapsulated lesion composed of ducts w/papillary projections
- Some ducts connect to epithelium
- Lined by apocrine cells w/myoepithelial layer
- Stroma contains lymphocytes and plasma cells
- Likely tubular apocrine adenoma/SCP variant



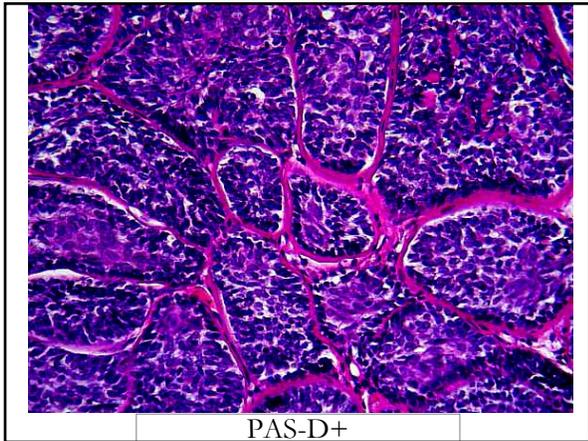
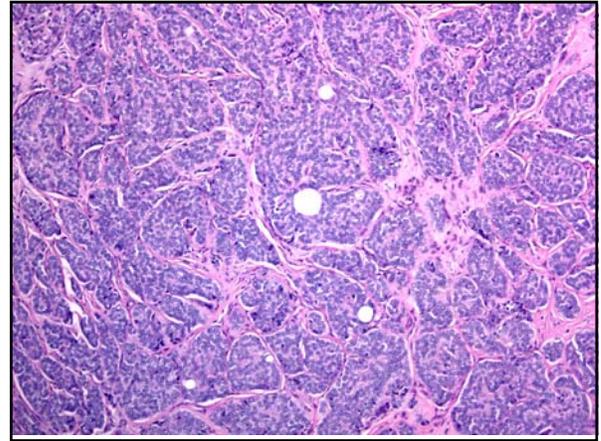
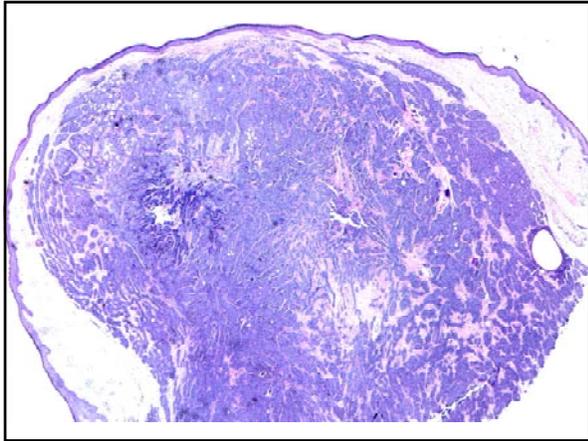
8. CYLINDROMA

Clinical:

- Small, solitary lesions on head and neck of mid-aged to elderly, F > M
- Multiple tumors (turban tumor) inherited as AD trait, a/w/trichoeps & eccrine spiradenoma (Brooke-Spiegler)

Histology:

- Poorly circum'd dermal tumors consisting of irregular nests and cords ("jigsaw puzzle") surrounded by hyaline membranes, membrane droplets in nests, PAS-D+
- Focal ductal, apocrine, or sebaceous diff'nt may be found
- Malignant cylindroma: very rare, loss of architecture, increased cellular pleomorphism, atypia, mitoses



PAS-D+

• DIFFERENTIAL DIAGNOSIS:

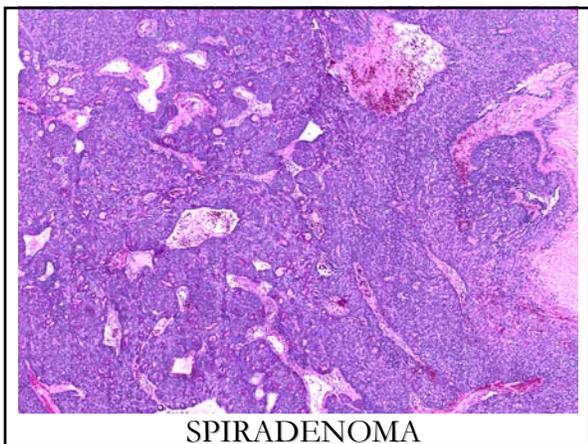
1. **Spiradenoma:**

- Cylindroma overlap with spiradenoma not uncommon, may see areas of both in the same tumor, or separate areas of distinct cylindroma and eccrine spiradenoma

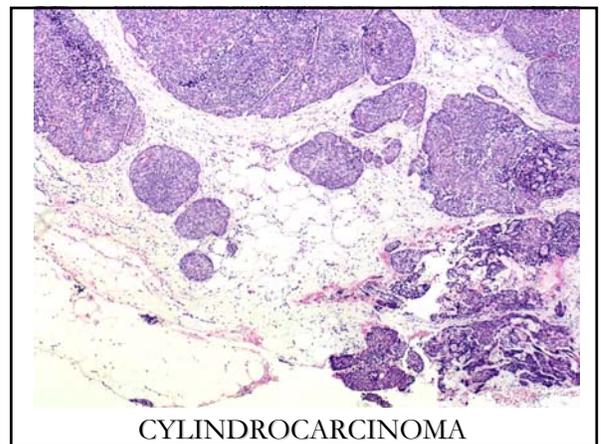
2. **Cylindrocarcinoma:**

- Rare tumor, usually see areas of benign cylindroma, w/areas of poorly diff'nt, infiltrating tumor

- More common in cylindromatosis; aggressive behavior w/freq mets



SPIRADENOMA



CYLINDROCARCINOMA

9. ADENOID CYSTIC CARCINOMA

Clinical:

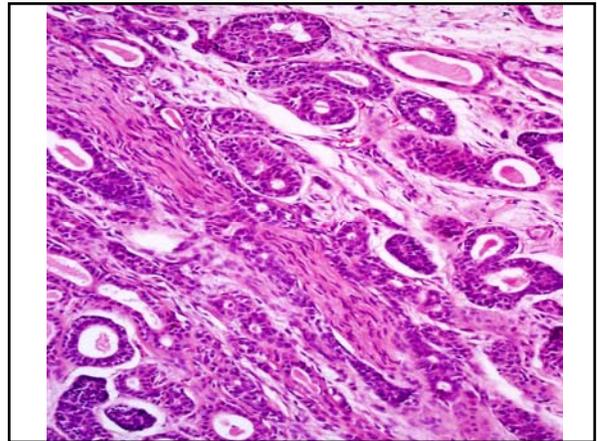
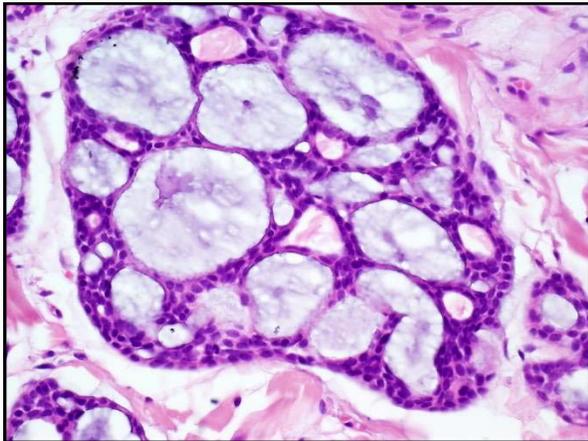
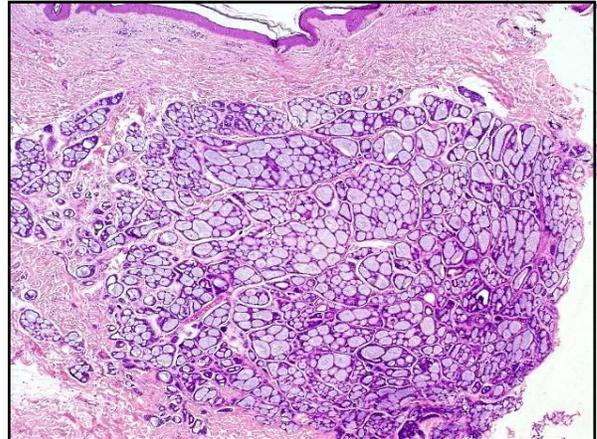
- Rare primary cutaneous tumor, often scalp or chest
- May arise from ceruminous and other apocrine glands

Histology:

- Islands and nests of cells with repetitive cribriform spaces and tubular areas filled with mucinous and basement membrane material
- Low grade histology, rare mitoses, but frequent perineural invasion

Prognosis:

- Indolent growth and high recurrence potential (up to 70%), but low metastatic rate



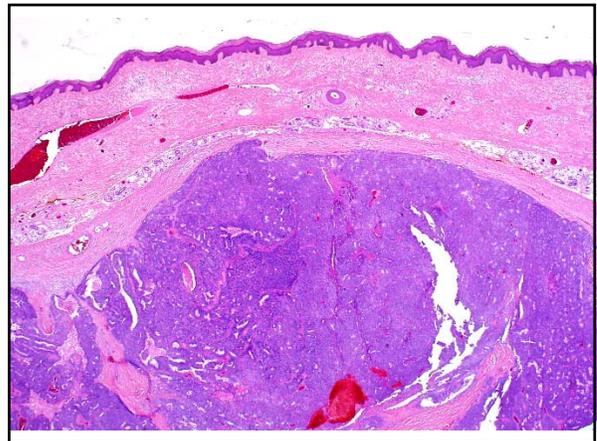
10. AGGRESSIVE (DIGITAL) PAPILLARY ADENOCARCINOMA

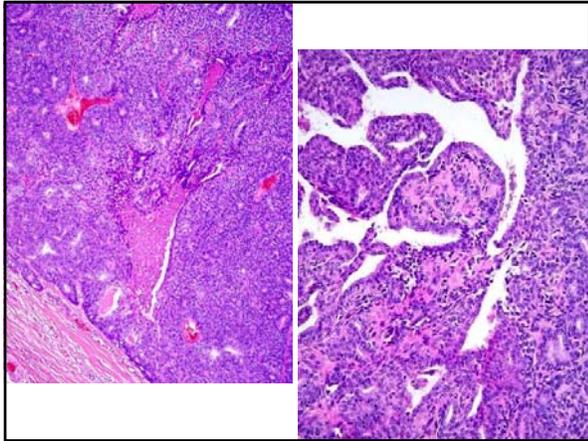
Clinical:

- Solitary painless, nodular/cystic mass on fingers or toes, usually < 2 cm, mostly in males
- Formerly divided into aggressive papillary adenoma and carcinoma, but all are malignant w/aggressive growth: recurrence in 50%, distant mets in 15% (usu. lungs)

Histology:

- Large, poorly circum. dermal/subcutaneous mass forming tubuloalveolar structures and cysts w/papillary projections
- Show a range of atypia, pleomorphism, and mitoses
- Stroma varies from thin fibrous septae to dense hyalinized collagen





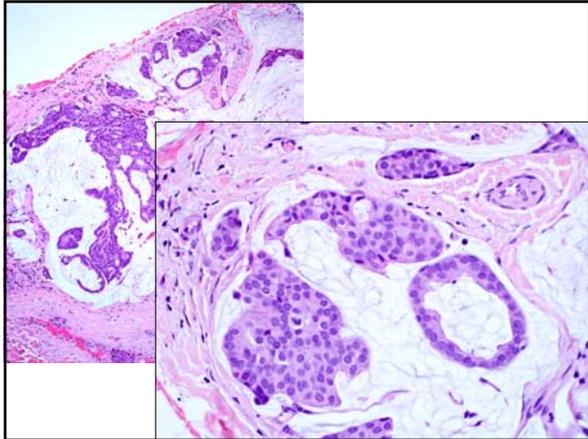
11. PRIMARY CUTANEOUS MUCINOUS CARCINOMA AND ENDOCRINE MUCIN-PRODUCING SWEAT GLAND CARCINOMA

Clinical:

- Rare, slow growing tumors, often present on face, scalp and eyelids (esp. mucin-producing tumors)
- Aggressive: mets in about 15% cases

Histology:

- Islands of epithelioid cells floating in pools of mucin (sialomucin), separated by thin fibrovascular septae
- Cells are generally small, cuboidal, may have neuroendo- crine diff'nt (chromo, synapto+)
- May express apocrine markers, CEA, EMA and S100, and strongly express ER/PR
- Must R/O met mucinous Ca (colon, breast, gyn)



V. CLASSIFICATION OF ECCRINE TUMORS

• Tumors of likely eccrine differentiation:

- Eccrine spiradenoma/spiradenocarcinoma
- Syringoma
- Eccrine syringofibroadenoma
- Papillary "eccrine" adenoma

• Tumors of questionable/occasional eccrine diff'nt:

- "Eccrine" poroma
- "Eccrine" hidradenoma
- Cylindroma
- Microcystic adnexal carcinoma (likely FSAU-derived)

- Eccrine carcinoma (syringoid carcinoma)

1. ECCRINE SPIRADENOMA

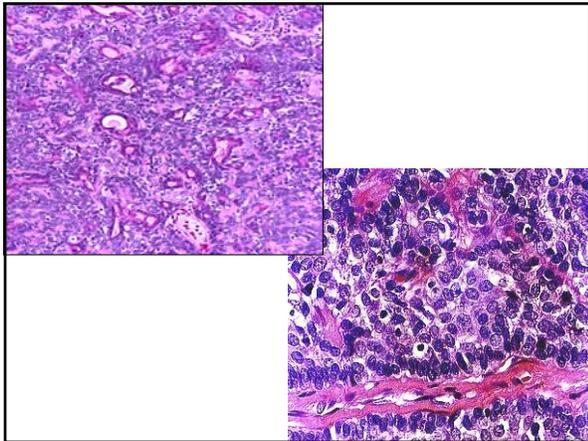
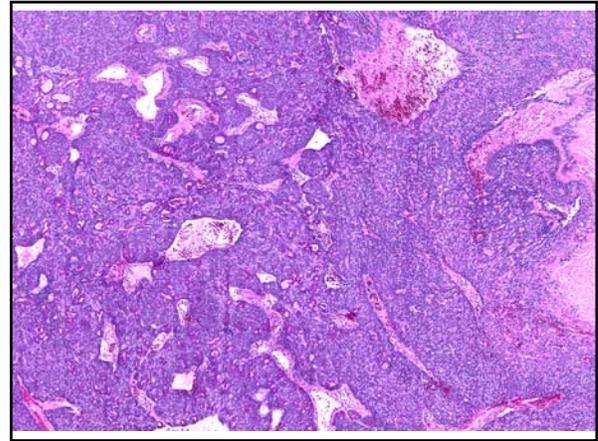
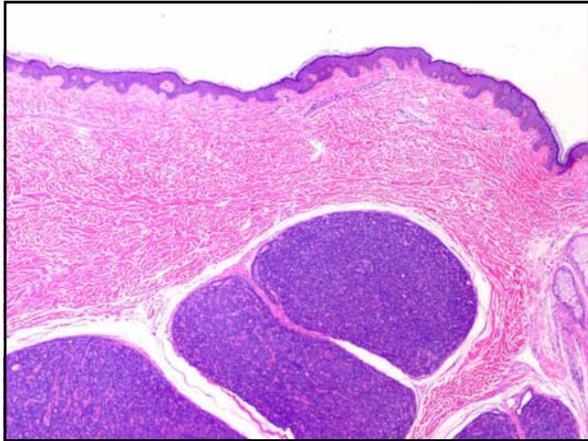
Clinical:

- Solitary nodule, 1-2 cm, varied locations, usually young adults, may be painful ("E" in "ANGEL" tumors)
- Rarely, multiple lesions or several lesions in zosteriform distribution, may be part of Brooke-Spiegler syndrome



Histology:

- One to several well-circumscribed dermal nodules, may have slight fibrous capsule, may be cystic and have prominent vascular spaces and hemorrhage
- Cells arranged in large nodules composed of small lobules and intersecting cords with ductal structures containing hyalinized material
- 2 cell population: small dark peripheral cells, larger, pale cells around lumina
- May have associated cylindroma in some cases



MALIGNANT SPIRADENOMA

Clinical:

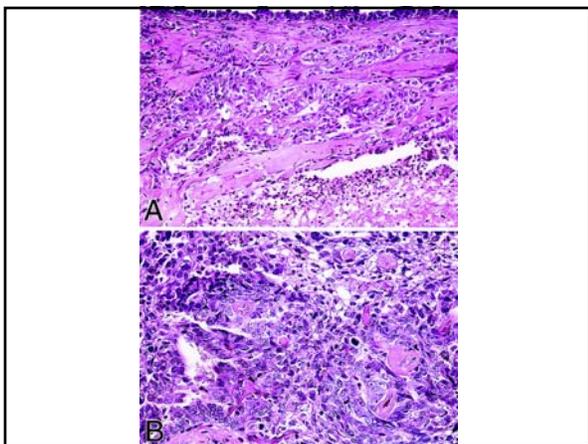
- Usually malignant transformation of large, untreated spiradenoma; clin history of sudden enlargement of long-standing lesion

Histology:

- Areas of benign-appearing spiradenoma and areas of malignant transformation with cellular atypia, nuclear hyperchromasia and pleomorphism, many mitoses

Prognosis:

- Mets occur, usually LNs, but few reported deaths



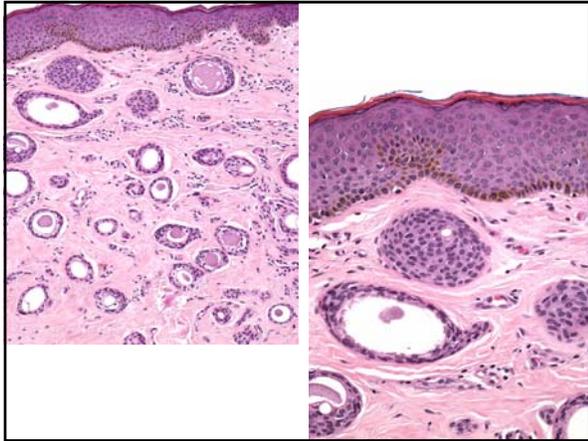
2. SYRINGOMA

Clinical:

- Occurs mostly on face, neck and upper trunk, young adults, F > M, Asians
- Usually multiple, variants include solitary, plaque-like, milia-like, genital, and eruptive (assoc. w/Down synd.), clear cell (assoc. w/diabetes)

Histology:

- Proliferation of variegated ductal structures lined by 2-6 cell layers, with dense eosinophilic luminal material
- Cords and tubules common, but tadpole shapes are classic; associated desmoplastic stroma
- Lack the deep infiltration and perineural invasion of MAC
- "Malignant syringoma" likely unrelated



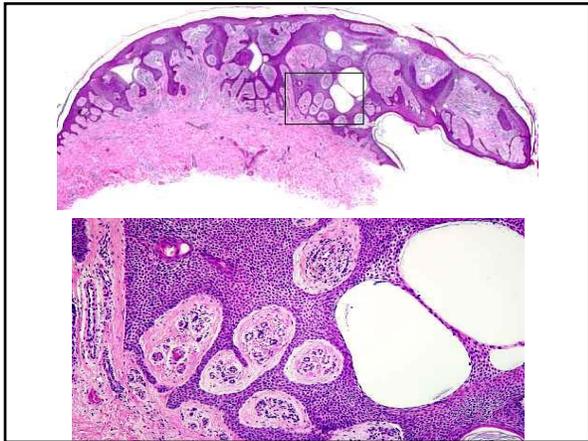
3. ECCRINE SYRINGOFIBROADENOMA

Clinical:

- Solitary, hyperkeratotic, nodule or plaque, usually on extremity
- Syringofibroadenomatosis: multiple lesions, a/w/PPK (e.g., hidrotic ectodermal dysplasia)
- Some cases likely reactive (adjacent inflammatory lesion or tumor); some assoc. w/HPV 10

Histology:

- Acanthotic tumor composed of narrow, anastomosing cords of bland acrosyringeal cells, usually with occasional lumina
- May show prominent clear cell change (glycogen)
- Fibrovascular stroma with chronic inflam infiltrate



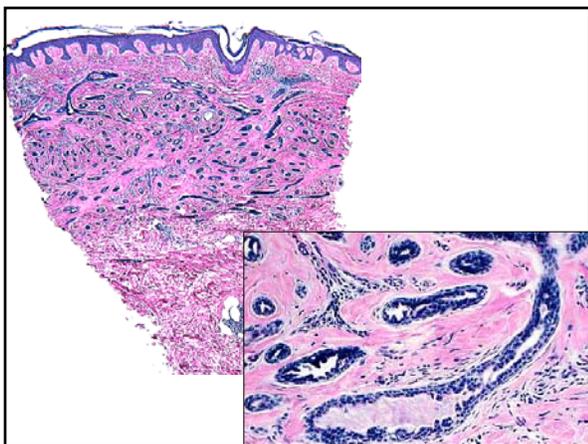
4. PAPILLARY “ECCRINE” ADENOMA

Clinical:

- Slowly growing firm nodule, preferentially affects extremities of black (female) patients
- Many cases probably represent tubular apocrine adenoma, but some cases show eccrine diff'nt

Histology:

- Circumscribed dermal tumor composed of dilated duct-like structures lined by 2+ layers of cells
- Inner layer forms intraluminal papillations, may show focal clear cell change
- Lumina may contain amorphous material



5. HIDRADENOMA

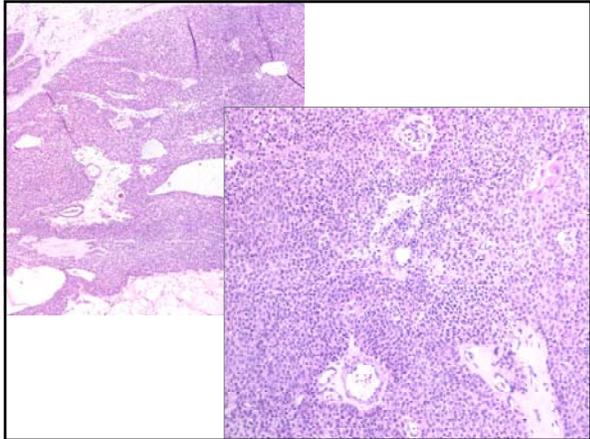
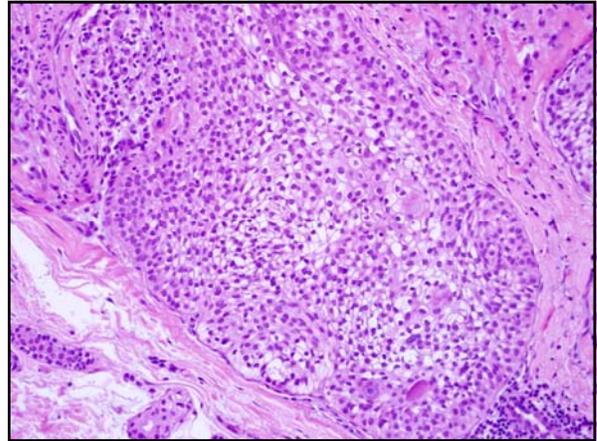
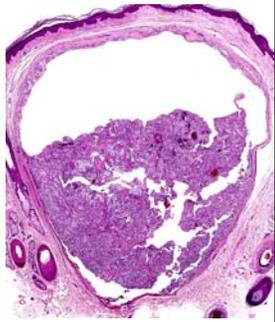
Clinical:

- Solitary, solid to partially cystic bluish nodule, F > M, usu. 1-2 cm, no site predilection
- Local recurrence fairly common, malignant transformation rare but aggressive (mets to LNs, lungs, bone)



Histology:

- Circumscribed but non-encapsulated, dermal-based nodule(s), may have epidermal connections (much fewer than poroma)
- Composed of bland eosinophilic to clear cells, often with squamoid different and, in some cases, apocrine and mucinous different (ductal areas)



HIDRADENOMA

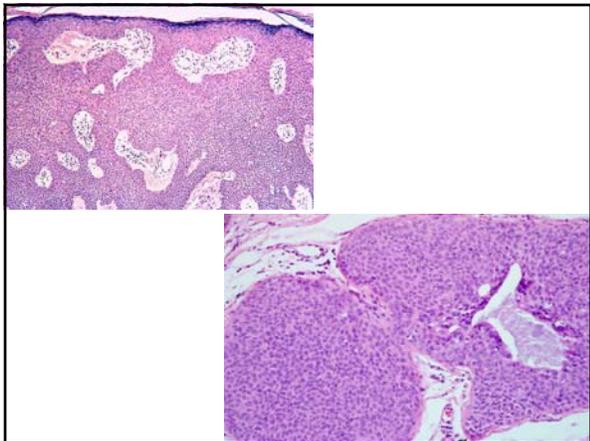
• DIFFERENTIAL DIAGNOSIS:

1. Tricholemmoma and Tricholemmal carcinoma

- Lobular configuration (perifollicular), with epidermal attachment, peripheral palisading, keratinization

2. Poroma

- Closely related (“eccrine acrospiroma”), attaches to the epidermis, composed of interanastomosing cords of small, bland adnexal keratinocytes; cases with overlap with hidradenoma



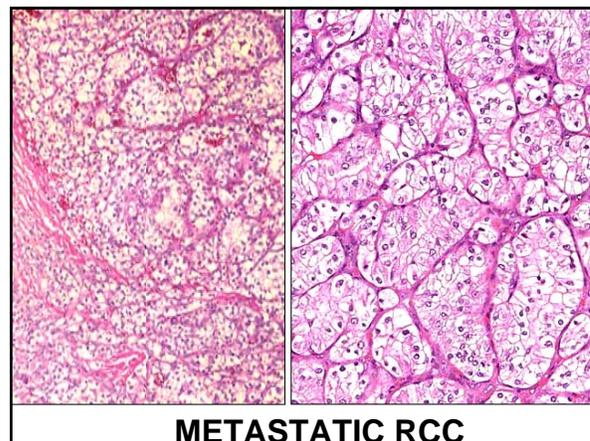
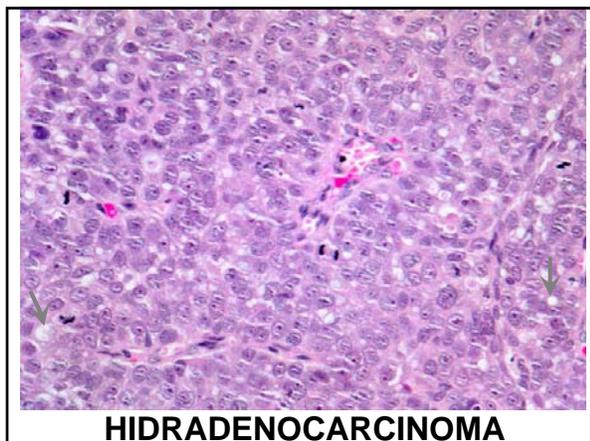
DIFFERENTIAL DIAGNOSIS:

3. Hidradenocarcinoma

- Usually see areas of typical benign hidradenoma, with other areas showing malignant features including infiltration, increased and atypical mitoses, and necrosis

4. Metastatic clear cell renal cell carcinoma

- May closely mimic clear cell hidradenoma, but shows more prominent vascularity and hemorrhage, may see prominent nucleoli but mitoses rare



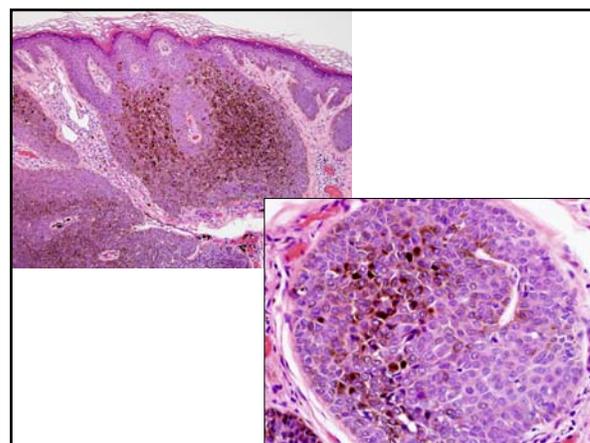
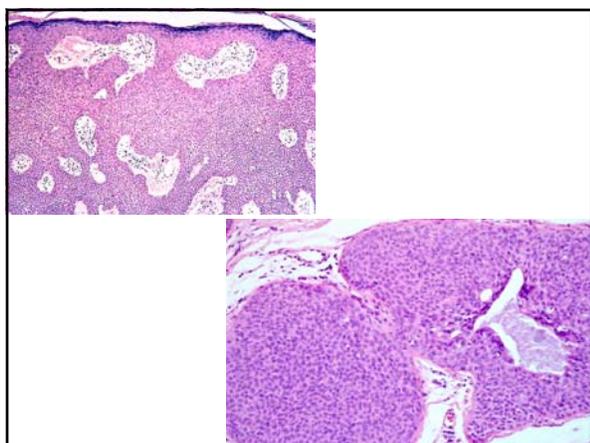
6. POROMA

Cinical:

- Foot, hands and fingers, but can occur anywhere
- Middle-aged patients
- Firm pink/red papule to nodule, asymptomatic

Histology:

- Broad, anastomosing strands of small, bland adnexal keratinocytes with intercellular bridges
- Focal ductal differentiation, often focal squamoid diff'nt, occasional sebaceous and apocrine diff'nt
- Cytoplasmic clearing may be present (glycogen)
- Stains: PAS+, CEA/EMA+ ductal lumens



POROMA VARIANTS:

1. Dermal duct tumor

- Monotonous tumor islands with focal ductal diff'nt located in the dermis, often with stromal sclerosis (not invasion)

2. Hidroacanthoma simplex

- Purely intraepidermal cellular lobules composed of bland poroid adnexal cells (one example of Borst-Jadassohn phenomenon)



POROMA

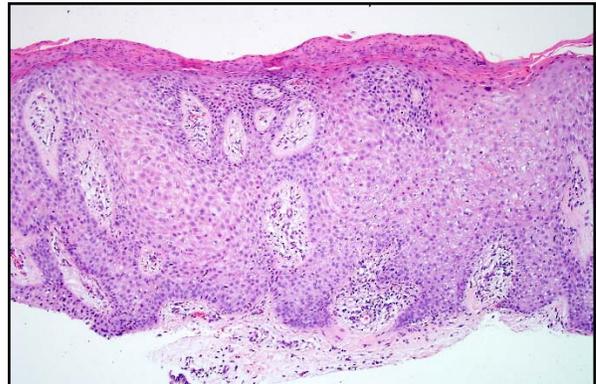
• DIFFERENTIAL DIAGNOSIS:

1. Tricholemmoma and Tricholemmal carcinoma

- Lobular configuration (perifollicular), with epidermal attachments, peripheral pallisading, keratinization

2. Clear cell acanthoma

- Likely reactive, psoriasiform hyperplasia with clear cell change due to glycogen; composed of squamoid keratinocytes with loss of granular layer and corneal neutrophil collections



CLEAR CELL ACANTHOMA

3. Porocarcinoma

Clinical:

- Older patients, often on lower extremities, usually associated with longstanding poroma

Histology:

- Elongated rete ridges and large islands with cystic areas and frequent central necrosis
- Large, eosinophilic cells with squamoid diff'nt, marked atypia, nuclear hyperchromasia, mitoses
- May be in situ, but dermal invasion often present

Prognosis:

- Local recurrences (17%), local mets in up to 20%, visceral metastases and death in 11% cases

