CONFLICTS

- I have no conflicts with the content of this lecture.
OBJECTIVES

• Understand the classification of malignant adnexal tumors
• Recognize malignant transformation
• Recall related genetic syndromes
CLASSIFICATION

- Follicular
- Sebaceous
- Apocrine
- Eccrine
BILOGIC BEHAVIOR

Benign
Malignant
Highly Malignant
BENIGN VS MALIGNANT

- Size, Symmetry, Circumscription
- Invasion of adjacent structures
- Cytological atypia, Mitotic figures, Architecture
- Metastasis present
<table>
<thead>
<tr>
<th></th>
<th>BENIGN</th>
<th>MALIGNANT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Growth type</td>
<td>Expansive</td>
<td>Infiltrating</td>
</tr>
<tr>
<td>Growth speed</td>
<td>Slow</td>
<td>Rapid</td>
</tr>
<tr>
<td>Stabilization</td>
<td>Frequent</td>
<td>Exceptional</td>
</tr>
<tr>
<td>Structure</td>
<td>Typical</td>
<td>Atypical</td>
</tr>
<tr>
<td>Mitoses</td>
<td>Rare Typical</td>
<td>Numerous Atypical</td>
</tr>
<tr>
<td>Evolution</td>
<td>Local</td>
<td>Local &amp; General</td>
</tr>
<tr>
<td>Metastasizing</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Local consequences</td>
<td>Variable (compressions)</td>
<td>Severe (infiltration)</td>
</tr>
<tr>
<td>General consequences</td>
<td>None (exceptions)</td>
<td>Constant</td>
</tr>
<tr>
<td>Spontaneous evolution</td>
<td>Usually favorable</td>
<td>Always fatal</td>
</tr>
<tr>
<td>Evolution after removal</td>
<td>No recurrences</td>
<td>Recurrences</td>
</tr>
</tbody>
</table>
BENIGN VS MALIGNANT

- Immunohistochemistry defines differentiation
  NOT malignancy
ADNEXAL VS EPIDERMAL

- Epidermal continuity
- Differentiation
- Immunohistochemistry
ADNEXAL VS METASTATIC

- Epidermal continuity
- Differentiation
- Multiple vs. solitary
- Immunohistochemistry (P63, ER/PR)
- Size, symmetry, circumscription
MALIGNANT TRANSFORMATION

- Malignant cylindroma
- Malignant eccrine poroma
- Malignant eccrine spiradenoma
- Malignant nodular hidradenoma
- Malignant chondroid syringoma
MALIGNANT TRANSFORMATION

- Malignant proliferating trichilemmal tumor
- Pilomatrix carcinoma
- Trichoblastic carcinoma
MALIGNANT TRANSFORMATION

- Pitfalls to diagnosis
  - Inadequate/insufficient sampling (shave)
  - Lack of differentiation
  - Benign and malignant components
  - Unable to recognized benign component
  - Metastatic lesion (Clinical history, P63, etc.)
MALIGNANT CYLINDROMA

- Elderly, slight female predominance
- Most frequently malignant transformation in the setting of multiple cylindromas (i.e. Brooke-Spiegler syndrome, CYLD)
- Follicular vs. eccrine/apocrine
- Invasion, atypia, mitoses, loss of hyaline sheath
- Frequent recurrence and metastasis
MALIGNANT POROMA (POROCARCINOMA)

- Elderly, M=F
- Legs and feet, eroded red nodule
- De novo or malignant transformation in a poroma
- Borst-Jadassohn pattern in epidermis
- Multiple cutaneous metastases
- Recurrence and metastasis common
BORST-JADASSOHN

- Clonal seborrheic keratosis
- Poroma
- Superficial basal cell carcinoma
- Squamous cell carcinoma in-situ
- Melanoma in-situ
- Junctional nevus
MALIGNANT SPIRADENOMA (SPIRADENOCARCINOMA)

- Young adults, M=F
- Malignant transformation of solitary spiradenoma
- Reported in Brooke-Spiegler syndrome (CYLD)
- Reported in breast
- Surgical excision
- Recurrence and metastasis common
MALIGNANT SPIRADENOMA (SPIRADENOCARCINOMA)
MALIGNANT NODULAR HIDRADENOMA (HIDRADENOCARCINOMA)

- Older adults, M=F
- De novo or malignant transformation
- Clear cell morphology (mimics renal cell Ca)
- Estrogen and progesterone receptors
- Recurrence and metastasis common
MALIGNANT NODULAR HIDRADENOMA (HIDRADENOCARCINOMA)
MALIGNANT CHONDROID SYRINGOMA
(MALIGNANT MIXED TUMOR OF THE SKIN)

- Wide age range, F>M, extremities
- De novo or malignant transformation
- Invasion, atypia, mitoses, satellite nodules, necrosis
- Very high rate of recurrence and metastasis
MALIGNANT CHONDROID SYRINGOMA
(MALIGNANT MIXED TUMOR OF THE SKIN)
CARCINOMAS WITH FOLLICULAR DIFFERENTIATION

- Malignant proliferating trichilemmal tumor
- Trichilemmal carcinoma
- Pilomatrix carcinoma
- Trichoblastic carcinoma
MALIGNANT PROLIFERATING TRICHILEMMAL TUMOR

- Elderly, sudden enlargement of scale nodule
- Malignant transformation of a proliferating trichilemmal cyst
- Marked cytological atypia
- Resembles squamous cell carcinoma
- Frequent recurrence and metastasis
MALIGNANT PROLIFERATING TRICHILEMMAL TUMOR
FOLLICULAR DIFFERENTIATION
TRICHILEMMAL CARCINOMA

- Elderly, face/ears, indurated plaque
- Unusual in Cowden's disease
- Infiltrative base with cytological atypia
- Periodic acid-Schiff positive clear cells
- Associated Pagetoid pattern occasionally
- Recurrence and metastasis uncommon
TRICHILOMMAmal CARCINOMA

FOLLICULAR DIFFERENTIATION
CLEAR CELL TUMORS

- Adnexal tumors
- Metastatic carcinomas
- Balloon cell nevus and melanoma
- Clear cell BCC and SCC
- Clear cell DF and AFX
- Salivary gland tumors
Glycogen-rich malignant melanomas and glycogen-rich balloon cell malignant melanomas: frequency and pattern of PAS positivity in primary and metastatic melanomas.
Nowak MA, Fatteh SM, Campbell TE.
Pilomatrix carcinoma

- Elderly, M>F
- De novo or malignant transformation of pilomatricoma
- Cellular basaloid tumor with atypia and mitoses
- Asymmetric and infiltrative
- Shadow cells and cystic necrosis
- Frequent recurrence and metastasis
TRICHOBLASTIC CARCINOMA

- Middle age to elderly, M=F
- Face and scalp > trunk and extremities
- Malignant transformation in a trichoblastoma
- Resembles basal cell carcinoma
- Frequent recurrence and metastasis
TRICHOBLASTIC CARCINOMA
FOLLICULAR DIFFERENTIATION
SEBACEOUS CARCINOMA

OCULAR TYPE
SEBACEOUS CARCINOMA

- Ocular Type
  - 75% of sebaceous carcinomas
  - < 1% of eyelid tumors
  - Upper eyelid, elderly, F>M
  - Most commonly arises from Meibomian glands
SEBACEOUS CARCINOMA

• Ocular Type
  • Easily mistaken for chronic chalazion
  • Frequent metastases and Pagetoid spread
  • Atypical cells with foamy cytoplasm (lipid)
  • Oil Red O positive, CEA/EMA positive
SEBACEOUS CARCINOMA
EXTRAOCULAR TYPE
SEBACEOUS CARCINOMA

• Extraocular Type
  • 25% of sebaceous carcinomas
  • Head and neck
  • May cause regional metastases
Muir Torre Syndrome

- Variant of Lynch syndrome
- Sebaceous tumors and keratoacanthomas
- Visceral malignancies (colorectal, GU)
- Mutations in DNA mismatch repair genes and microsatellite instability (MSH-2, MLH-1, MSH-6, PMS-2)
CARCINOMAS WITH APOCRINE DIFFERENTIATION

- Apocrine carcinoma
- Extramammary Paget’s Disease
APOCRINE CARCINOMA

Very Rare

Axilla and other sites of high apocrine gland density

Adenocarcinoma

D/D Metastatic Breast CA
EXTRAMAMMARY PAGET'S DISEASE

- Vulva most common
- Male genital area
- Perianal area
- Axilla
Perianal Paget's disease: distinguishing primary and secondary lesions using immunohistochemical studies including gross cystic disease fluid protein-15 and cytokeratin 20 expression.

Nowak MA, Guerriere-Kovach P, Pathan A, Campbell TE, Deppisch LM.

Grelck KW, Nowak MA, Doval M.
EXTRAMAMMARY PAGET’S DISEASE

- Sharply demarcated erythematous patch
- Pruritus common
- Primary vs. secondary
EXTRAMAMMARY PAGET’S DISEASE

INTRAEPIDERMAL APOCRINE CARCINOMA
CYTOKERATIN 7 POSITIVE
PAGETOID PATTERN

- Paget’s/Extramammary Paget’s disease
- Melanoma/Melanoma in-situ
- Squamous cell carcinoma in-situ
- Sebaceous carcinoma
- Pagetoid reticulosis
CARCINOMAS WITH ECCRINE DIFFERENTIATION

- Classic type eccrine carcinoma
- Syringoid eccrine carcinoma
- Microcystic adnexal carcinoma
- Mucinous eccrine carcinoma
- Mucoepidermoid carcinoma
- Adenoid cystic carcinoma
- Agressive digital papillary carcinoma
CLASSIC TYPE ECCrine ADENOCARCINOMA

- Head and neck region
- High incidence of metastases
- Tubular structures with highly anaplastic areas
- Difficult to distinguish from metastatic carcinoma
CLASSIC TYPE ECCrine CARCINOMA

Resembles other types of adenocarcinoma
SYRINGOID ECCRINE CARCINOMA

- Head and Neck
- Low metastatic rate
- Infiltrative with ductal and cystic components
- Perineural invasion and recurrence common
Syringoid Eccrine Carcinoma

- Head and neck
- Low metastatic rate
- Recurrence common
SYRINGOID ECCrine CARCINOMA
Deeply infiltrative
SYRINGOID ECCRINE CARCINOMA

Ductal and cystic areas

Comma and tadpole forms

Perineural involvement
Microcystic Adnexal Carcinoma

Middle-aged adults, F > M

Upper lip

Recurrence common

Metastasis rare
MICROCYSTIC ADNEXAL CARCINOMA

Deeply infiltrative
MICROCYSTIC ADNEXAL CARCINOMA

- Desmoplastic stroma
- Horn cysts in upper dermis
- Thin cords of deceptively bland cells
- Perineural invasion
- D/D Trichoepithelioma (CD23)
MUCINOUS ECCRINE CARCINOMA

Elderly, F > M

Head and neck, eyelid 30-40%

Recurrence common

Metastasis rare
MUCINOUS ECCRINE CARCINOMA

Strands of fibrous tissue

Islands of atypical cells in a sea of mucin

Eccrine vs. Apocrine

D/D metastatic carcinoma
Mucoepidermoid Carcinoma

- Mixture of squamous and glandular (low-grade adenosquamous carcinoma)
- Identical to mucoepidermoid carcinoma of salivary glands
- Distinct from high grade adenosquamous carcinoma (separate components)
ADENOID CYSTIC CARCINOMA

- Indolent compared to its salivary gland counterpart
- Perineural involvement and recurrence common
- Metastasis uncommon
- Adenoid & cribriform patterns
- D/D: BCC vs parotid tumor
AGGRESSIVE DIGITAL PAPILLARY CARCINOMA

- Hands & feet, fingers & toes
- Young adults, M > F
- Metastasis common
AGGRESSIVE DIGITAL PAPILLARY ADENOCARCINOMA

- Cellular dermal nodule
- Well circumscribed
- Papillary architecture
- Cystic lumina
AGGRESSIVE DIGITAL PAPILLARY ADENOCARCINOMA

- Cytological atypia & mitoses
- Can be deceptively bland
- D/D Metastatic Carcinoma
TAKE-HOME MESSAGES

- Adequate sampling is absolutely key (i.e., MAC)
- Metastatic carcinomas can be mistaken for adnexal carcinomas
- Malignant transformation can occur in preexisting benign tumors
SEBACEOUS CARCINOMA

- Most commonly arise from Meibomian glands
- Upper eyelids > Lower eyelids
MUIR-TORRE SYNDROME

- Sebaceous tumors and GI/GU malignancies
- MSH-2 most common mutation
EXTRAMAMMARY PAGET’S DISEASE

- Apocrine differentiation and CK7 positive
- Primary vs. secondary (CK20, MUC-2)