Apocrine and eccrine adnexal tumors

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Past misguided notions

- Syringoma is eccrine
- Eccrine poroma – rather than eccrine or apocrine poroma
- Spiradenoma is eccrine while its sibling cylindroma is apocrine
- Microcystic adnexal carcinoma shows mixed follicular and eccrine differentiation
Guest Editorial

A Call for Logic in the Classification of Adnexal Neoplasms

Timothy H. McCalmont, M.D.
Factors crucial to the evaluation of adnexal lineage

- Embryology
- Combined and associated tumors
- Anatomic distribution
- Morphology & phenotype
  - By light microscopy, EM, and immunostaining
Embryology.
Apocrine differs from eccrine
Folliculo-sebaceous-apocrine unit
Does ontogeny reflect phylogeny?

- Alleged combinations of eccrine and follicular (or eccrine and sebaceous) are probably fictional
Syringocystadenoma papilliferum
Nevus sebaceus and secondary neoplasms

- Syringocystadenoma (apocrine)
- Trichoblastoma (follicular)
- Trichilemmoma (follicular)
- Sebaceous adenoma (sebaceous)
- Tubular adenoma (apocrine)
- Poroma (apocrine, when occurring in nevus sebaceus)
Combined tumors.
Combined tumors

• Elements that commonly occur conjointly, non-coincidentally, are of related lineage

• Example: glomangiomyoma
Combined adnexal tumors

- Spiradenoma and cylindroma
- Spiradenoma and trichoepithelioma
- Cylindroma and trichoepithelioma
- Tubular adenoma and sebaceous adenoma
Spiradenoma
Cylindroma
Q.E.D.

- Trichoepithelioma, spiradenoma, and cylindroma are all folliculosebaceous-apocrine
Neoplastic associations (syndromic)
Spiradenomas in Brooke–Spiegler Syndrome

W. Weyers, M.D., M. Nilles, M.D., F. Eckert, M.D., and W.-B. Schill, M.D.
What’s the lesson of Brooke-Spiegler?

- The combination of spiradenoma with cylindroma and trichoepithelioma in a genetic syndrome indicates folliculosebaceous-apocrine lineage
Anatomic distribution.
Distribution of adnexa

- The distribution of adnexal tumors parallels the structures toward which they differentiate
Trichoblastoma
(trichoepithelioma)
Trichoblastoma

- Sex: 72:28 (F>M)
- Age: 3-99 years
- head/neck: 96%
- arm/leg: 4%
- hand/foot: <1%
Syringoma

- Sex 79:21 (F>M)
- Age 17-88 yrs
- head/neck 90%
- axilla/genital 5%
- arm/leg 5%
- hand/foot <1%
Acral Syringoma

Philip S. H. Hughes, MD, Prapand Apisarnthanarax, MD

(Arch Dermatol 113:1435-1436, 1977)
Spiradenoma

- **Sex**: 53:47 (F>M)
- **Age**: 14-96 years
- **head/neck/trunk**: 76%
- **arm/leg**: 24%
- **hand/foot**: <1%
Houston, we have a problem.

- If spiradenoma or syringoma were purely eccrine, we’d see them as palmoplantar tumors
Morphology.
Morphologic attributes

- Light microscopic pattern
- Immunophenotype (immunohistochemistry)
- Enzyme expression (histochemistry)
- Ultrastructure (electron microscopy)
Least Common Denominators for Diagnosis
Follicular attributes

- Basaloid (germinative) cells with adjacent mesenchymal cells (resembling the bulb and papilla)
- Matrical (“shadow”) cells
- Pallid (outer sheath) cells with adjacent thickened membrane
- Trichohyaline granules
Sebaceous attributes

- Cells with coarsely vacuolated cytoplasm and scalloped nuclei
Apocrine attributes

- “Decapitation”? 
- Cuticulated ducts?
- Pallid (clear) cells?

Eccrine attributes

- Cuticulated ducts?
- Pallid (clear) cells?
Immunohistochemical reagents

- Carcinoembryonic antigen (CEA)
- S100 protein
- Gross cystic disease fluid protein (GCDFP-15)
- Epithelial membrane antigen (EMA)
- Anti-keratins
Morphologic conclusions

- We can precisely define follicular and sebaceous differentiation
- We cannot precisely identify apocrine and eccrine lineage
Morphologic conclusions

- The distinction and classification of apocrine and eccrine lesion requires integration of a variety of factors, including embryology, distribution, and microscopy.
Eccrine Neoplasms

- Less common than apocrine, probably because
  - ... of the monophasic nature of the eccrine apparatus
  - ... of little proliferative potential (hyperproliferation precedes mutagenesis in oncogenesis)
Eccrine tumors

- Syringoma, sometimes
- Poroma, commonly
- Hidradenoma, sometimes
- Papillary adenoma, commonly
Poroma

• Of eccrine or apocrine lineage
  • … of palm or sole, manifest as a vascular nodule: “eccrine” poroma
  • … within nevus sebaceus or on axillary skin: “apocrine” poroma
Poroma

- Patterns
  - *Juxtaepidermal* (epidermal and dermal poroma)
  - *Intraepidermal* (hidroacanthoma simplex)
  - *Intradermal* (dermal duct tumor)
Poroma

- **Hallmarks**
  - Small cuboidal ("poroid") cells
  - Prominent ductular differentiation
  - Highly vascular stroma
  - Necrosis en masse, sometimes
Papillary adenoma

• A “proliferative” adenoma, with tubules lined by a cellular multi-layered epithelium from which papillary projections extend into the luminal space

• Eccrine or apocrine in lineage
“Aggressive” (digital) papillary adenoma
“Aggressive” papillary adenoma

• In retrospect, most examples represent malignancy, i.e. papillary adenocarcinoma

• Of course an ‘adenoma’ may seem aggressive if it is truly an adenocarcinoma
Apocrine tumors

- Apocrine differentiation often occurs jointly with follicular and sebaceous attributes, *thus diverse!*
- Strictly apocrine lesions are often indistinguishable from strictly eccrine neoplasms via conventional microscopy
Strictly apocrine tumors

- Syringoma, commonly
- Poroma, commonly
- Hidradenoma, commonly
- Apocrine adenomas, including hidradenoma papilliferum and syringocystadenoma
- Spiradenoma and cylindroma
Tumors with apocrine-follicular (or folliculosebaceous-apocrine) differentiation

- Chondroid syringoma (mixed tumor)
- Microcystic adnexal carcinoma
Syringoma

- Occur at virtually any site; commonly periorbital
- Uncommon at acral or glabrous sites
- Apocrine or eccrine in lineage; most are probably apocrine
- Usually small, often characterized by considerable sclerosis
Syringoma

- **Hallmarks**
  - Numerous small nests or ducts, often with a central cuticle
  - Enveloping sclerotic stroma
  - Tadpole or comma-shaped nests, sometimes
Hidradenoma

- Close relative of poroma
- Usually dermal, usually composed of cells with ample pale eosinophilic cytoplasm (“clear cell” hid.)
- May be cystic (“solid-cystic” hid.)
- Eccrine or apocrine in lineage; most are apocrine
“Acrospiroma”

• Bridging designation that encompasses poroma and hidradenoma

• Equivalent to the garbage can designation “nodular hidradenoma”
Hidradenoma

- **Hallmarks**
  - Cuboidal cells, often with pale cytoplasm and generally larger than those of poroma
  - Limited ductular differentiation
  - Solid or cystic or both
  - Stromal sclerosis, often
Apocrine adenomas

- Papillary adenoma
- Tubular adenoma
- Tubulopapillary adenoma
- Hidradenoma papilliferum
- Syringocystadenoma
Hidradenoma papilliferum

- A papillary adenoma of apocrine lineage with a circumscribed but frond-like pattern
- Occur on genital skin or in the axillary vault, commonly
- Unrelated to conventional (simple) hidradenoma
Apocrine adenoma spectrum

- Tubular adenoma
- Papillary adenoma
  - Hidradenoma papilliferum
- Tubulopapillary adenoma
- Syringocystadenoma papilliferum
- Periocular apocrine adenoma
Spiradenoma

- A tumor with primitive glandular and little ductular differentiation
- Simply spiradenoma (not eccrine spiradenoma)
Apocrine spiradenoma!

- Non-volar
- Coexists with cylindroma
- Occurs in the breast
- Coexists with trichepithelioma in Brooke-Spiegler syndrome
- All suggest folliculosebaceous-apocrine lineage
Spiradenoma

- Has a child’s jigsaw puzzle pattern with only a few pieces arrayed in non-complex fashion
- A trabecular pattern within nodules, with “dark” peripheral cells and pale central cells
- Superimposed lymphocytes
Cylindroma

- Also neoplasm of apocrine lineage with primitive glandular differentiation
Multinodular cylindroma ("turban tumor")

(Weyers et al)
Cylindroma

- Has an adult jigsaw puzzle pattern with 500 interlocking pieces arrayed in a complex pattern
- Often deposition of basement membrane material in small “droplets” within nests or circumferentially around nests
Mixed tumor (chondroid syringoma)

- A hamartoma-like proliferation with tubular and ductular epithelial structures enveloped by equal proportions of mesenchyme
- Stroma may be cartilaginous ("chondroid"), myxoid, fibrocytic, adipocytic, or a mix
Mixed tumor

- Most (90%) display prominent apocrine differentiation
- May observe follicular germinative, outer sheath, isthmic or infundibular, or sebaceous diff.
- AKA: *pleomorphic adenoma*
Am J Dermatopathol 1992; 14:186-94:

Apocrine type of cutaneous mixed tumor with follicular & sebaceous differentiation.

Requena L et al
**Mixed tumor**

- Mixed tumors may also show strictly ductular differentiation, uncommonly
Microcystic adnexal carcinoma (MAC)

- Rare, but among the most common adnexal carcinomas
- Presents on the head and neck, most commonly
- Slow growing, with onset often back-dated to 20s or 30s
MAC

- Typified by combined follicular and glandular differentiation
- Cytologically bland but architecturally malignant and infiltrative
- Prone to misdiagnosis, especially in superficial biopsies
MAC

• **Hallmarks**
  • Poor circumscription with deep infiltration, often of nerve or muscle
  • Stromal desmoplasia
  • Follicular differentiation, commonly microcystic (infundibular)
  • Ductular differentiation, commonly syringomatous
  • (Remember that syringomatous carcinoma is half a MAC)