Overview

- Epithelioid sarcoma
- Rhabdoid tumor
- Epithelioid malignant peripheral nerve sheath tumor
- Myoepithelioma
- Extra-axial chordoma
- Epithelioid hemangioendothelioma
- Epithelioid hemangiomma
- Epithelioid sarcoma-like/pseudomyogenic hemangioendothelioma

Epithelioid Sarcoma

- Classical ES typically presents as a small, superficial lesion of the distal extremities in adolescents and young adults
- Proximal-type ES occurs as a large, deep mass in older adults

Pathological Features

- Nodular, vaguely circumscribed but infiltrative
- Garland-like appearance with necrosis
- Relatively bland epithelioid cells
- Modulates from epithelioid to spindled
- PTES shows greater pleomorphism, rhabdoid cells, geographic necrosis
- Variants with chronic inflammation, hyalinized collagen, bone, myxoid or pseudovascular change
Inflammatory Myxoid Calcifying Pseudoglandular

Proximal-type ES
Immunohistochemistry

- LMWCK, HMWCK, EMA-positive
- Vimentin co-expression
- CD34 expression (50-60%)
- SMARCB1 loss (90%)
- Generally negative for more specific endothelial markers (CD31, FLI1/ERG)
- Generally negative for p63 and p40

Outcome

- Not graded by either French or NCI systems
- Over 70% recur and nearly 50% metastasize
- Often recur in more proximal soft tissue as multiple nodules
- Adverse prognostic factors include male sex, proximal location, size > 5cm, deep location
- Proximal variant may metastasize earlier

SMARCB1

- Ubiquitously expressed gene located on chromosome band 22q11.2
- Also known as INI1, SNF5, BAF47
- Part of the SWI/SNF chromatin remodeling complex
- Regulates gene expression by displacing DNA from histones and allowing transcription

SMARCB1-Deficient Tumors

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>SMARCB1-Negative</th>
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<tbody>
<tr>
<td>Epithelioid Sarcoma</td>
<td>~ 90%</td>
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<tr>
<td>Rhabdoid tumor</td>
<td>100%</td>
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<tr>
<td>Renal medullary CA</td>
<td>100%</td>
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<tr>
<td>Myoepithelial CA</td>
<td>10-40%</td>
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<tr>
<td>Extracellular myxoid CS</td>
<td>~ 20%</td>
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SMARCB1 in Rhabdoid Tumor
Malignant Rhabdoid Tumor

- Beckwith and Palmer (1978) originally regarded as "rhabdomyosarcomatoid variant of Wilms' tumor."
- Renal, CNS (atypical teratoid/rhabdoid tumor, AT/RT), soft tissue (malignant extrarenal rhabdoid tumor, MERT) and disseminated presentations
- Renal MRT and AT/RT: children < 1 year of age; aggressive clinical course
- Disseminated MRT: often lack clear primary tumor; may be part of familial rhabdoid tumor predisposition syndrome
- MERT
  - Deep axial locations, paraspinal region and neck
  - Much broader age range than renal MRT, although still far more common in children
  - Vimentin-positive; less often CK-positive
  - Usually CD34-negative
  - Aggressive clinical behavior, with <50% of patients alive at 5 year

MERT: Entity or Pattern?

- Rhabdoid phenotype may be seen in essentially any tumor
- Has been suggested that many MERT in adults represent other tumors, especially proximal-type epithelioid sarcoma

INI1 expression is retained in composite rhabdoid tumors, including rhabdoid meningiomas
Epithelioid MPNST

- < 5% of MPNST
- Composed predominantly or exclusively of epithelioid Schwann cells
- M/F; 20–50 years of age
- Usually involve major nerves
- Less often NF1-associated than are conventional MPNST
- Most common subtype of MPNST arising within schwannomas

- Nests and cords of epithelioid cells with prominent nucleoli
- Variable myxoid change and a minor degree of spindling
- Intensely S100 protein-positive, abundant pericellular collagen IV, negative for melanoma-specific markers
- Frequently SMARCBI-deficient
- Aggressive tumors with 50% metastatic risk; may metastasize to lymph nodes
Myoepithelioma

- Parachordoma described initially by Laskowski (1951), and more fully by Dabska (1977); controversial and rare
- Myoepithelioma/mixed tumor of soft parts described by Kilpatrick et al (1997); relatively large number of subsequent reported cases
- The WHO currently considers both terms to be essentially synonymous

Clinical Features

- Adults in 2nd-4th decades of life (mean 35-38 years)
- No sex predilection
- Subcutis or deep soft tissues of the thigh, calf, arm, head/neck
- Painless mass
- All have potential for recurrence and/or metastasis
- Histologically benign tumors may metastasize
- Histologically malignant tumors have a greater risk of distant metastases
- Wide excision; unclear role for adjuvant therapy

Pathological Features

- Circumscribed but often subtly infiltrative, vaguely lobular
- Cords, chains and nests of spindled to epithelioid cells in a myxoid/chondroid matrix
- Hepatoid, glomoid, plasmacytoid and vacuolated ("physaliferous") cells
- Cytologic atypia, mitotic activity, vascular invasion, necrosis in a minority of cases
- Positive for cytokeratins and S100 protein; less often positive for muscle markers, p63 and GFAP; brachyury-negative
• EWSR1 rearrangements present in 45% of cases
  - EWSR1-POU5F1, EWSR1-PBX1, EWSR1-ZNF444, EWSR1-??

• PLAG rearrangements, characteristic of salivary gland pleomorphic adenoma, found only in “true” mixed tumors with ductal differentiation
Extra-axial Chordoma

- Extraordinarily rare
- Pathologically identical to axial chordomas
- Co-express cytokeratins and S100 protein
- Brachyury expression distinguishes from EMC, myoepithelioma, carcinoma
- May recur locally but have not as yet been reported to metastasize

Epithelioid Hemangioendothelioma

- Originally recognized in the lung (intravascular bronchioloalveolar tumor) and in the liver (sclerosing cholangiocarcinoma)
- Endothelial derivation and natural history first described by Weiss and Enzinger (1982)

Clinical Features

- Any age group; extremely rare in children
- No sex predilection
- Occurs in soft tissues, skin, viscera, bone
- Association with blood vessel in 50-60% of cases
- May present with symptoms related to vascular obstruction
- Metastasize in 10-25% of cases to lymph nodes, lung, soft tissue, liver, bone
### Pathological Features

- Myxochondroid to hyalinized matrix
- Single file, cord-like and sheet-like growth
- Small, bland epithelioid cells
- Intracytoplasmic lumen formation
- Rare mitotic figures
- Rare spindled cases
- "High-grade" or "malignant" tumors with high nuclear grade, frequent mitoses, necrosis (in association with areas of typical EHE)
- Positive for CD31, CD34, FLI-1, occasionally for cytokeratins
Epithelioid Hemangioma

- Uncommon benign or possibly reactive endothelial tumor, frequently identified in association with a damaged vessel
- "Angiolymphoid hyperplasia with eosinophilia"
- Head and neck; may be multiple
- Most often in dermis or subcutis; rarely in deeper locations
- Young adults; more common in women
- Skin lesions tend to be small; bone and soft tissue lesions may be large and cellular
- Requires only simple excision
Pathological Features

- Damaged, centrally located blood vessel in 60%
- Vaguely lobular growth pattern
- Eosinophils and lymphocytes
- Epithelioid endothelial cells
  - Abundant eosinophilic cytoplasm
  - “Tombstone” pattern
  - Intracytoplasmic vacuoles
  - Enlarged, normochromatic nuclei
- Mitotic figures may be present
• FOS rearrangements found in roughly 1/3rd of cases
• More common in bone and soft tissue; rare in skin
• All cases showing classical “angiolymphoid hyperplasia with eosinophilia” pattern were negative

Epithelioid Sarcoma-like/ Pseudomyogenic Hemangioendothelioma

• Extraordinarily rare
• Skin and subcutis
• Mimics ES or some type of myoid tumor
• Young adults; no sex predilection
• Small dermal nodule, seldom ulcerated
• May be multifocal and involve bone
• Cytokeratin-positive; expresses all endothelial markers except CD34
• SERPINE1-FOSB fusion
• Recurs locally; low risk for distant metastasis