- Giant cells
- Marked atypia
❖ Vacuolated, clear cells, pleomorphism
❖ Regarded as Fuhrman grade 4 RCC
Melan A
Dx: perivascular epithelioid cell tumor (PEComa) – metastatic to the lung

Review of original RCC: same as the current PEComa

Lesson: STS may often arise outside of the soft tissues
Dx: Metastatic PEComa
PEComa - the essentials

❖ Neoplasm of perivascular epithelioid cell differentiation
❖ F:M (6:1), mean age 45
❖ Association with tuberous sclerosis complex
❖ Most in retroperitoneum, pelvis, uterus, GIT, somatic soft tissue, skin, bone
❖ Nested, uniform epithelioid cells, abundant granular cytoplasm, round nuclei, small nucleoli
❖ Spindle cells
❖ Occasional giant cells. Mitoses are rare
❖ Radial arrangement with vessels
❖ Sclerosing PEComa: cords of cells in densely collagenised stroma
❖ HMB45, Melan-A, MITF, muscle markers, focal S-100, TFE3 in a small subset, some c-kit
❖ Malignant PEComa: > 5cm, mitotic activity, necrosis, atypia, pleomorphism, infiltration
❖ Those lacking these features: rarely metastasize
❖ DDx: liposarcoma, leiomyosarcoma, RCC (epithelioid- clue: pleomorphism but few mitoses)
Woman 68, 3-4 week hx of a 20mm red nodule on the dorsum of left foot. Bleeding.

Skin ellipse with tumour nodule resected

Case 5
❖ Sheets of rounded cells. Small to intermediate size
❖ Variable patterns
❖ Many mitoses
❖ Mild nuclear variability, visible nucleoli in some cells. Not an even cell distribution

❖ Small amounts of pale or eosinophilic cytoplasm

❖ Epithelioid appearance in areas
❖ Some epithelioid areas
❖ Visible nucleoli
❖ Rhabdoid or plasmacytoid appearance
- Nucleoli
- Epithelioid, stromal myxoid change
- Mitoses
❖ Nested
❖ Myxoid
Infiltration of dermis
Ewing’s has uniform small round cells, with round nuclei, fine chromatin, scanty clear or eosinophilic cytoplasm. Indistinct cytoplasmic membrane. Some cytoplasmic clearing.
Additional Investigations

❖ CD99: multifocal reactivity, cytoplasmic & membraneous pattern, less diffuse and not the typical membranous pattern of Ewing’s sarcoma

❖ AE1/3, 34BE12, P63: Neg

❖ EMA, TLE1: Focal

❖ ERG, CD31: Neg

❖ INI-1: Retained

❖ S100: Neg

❖ Myoid markers: Neg

❖ CD138: Neg

❖ EWSR1 FISH: No rearrangement
Immunohistochemistry

NKX2.2 WT1
Progress & Final Dx: CIC Sarcoma

- Request for opinion & CIC FISH Dr CDM Fletcher
- CIC rearrangement confirmed. Has seen a number in the skin, mostly in older patients
- ETV4 IHC positive in a subset of cells
- The most common gene fusion is CIC-DUX4 (95%); CIC-FOXO4, CIC-LEUTX, CIC-NUTM1, and CIC-NUTM2A fusions in rare cases. 15% FISH negative, due to cryptic rearrangements. Immunohistochemical detection of ETV4 up-regulation is more sensitive than FISH for CIC
- Heterogeneous CD99, negative NKX2-2, and positive ETV4 and WT1 are characteristic immunophenotypic findings
- No targeted therapies. Treated like ES but worse outcome. Highly aggressive, more chemo-resistance, more frequent metastases
## IHC for Small Round Cell Sarcomas

**Acknowledgement:** Dr Jason Hornick

<table>
<thead>
<tr>
<th>Tumour</th>
<th>Keratin</th>
<th>Desmin</th>
<th>Myog</th>
<th>CD99</th>
<th>WT1</th>
<th>NKX2.2</th>
<th>ETV4</th>
<th>BCOR</th>
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<td>Ewing’s</td>
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</table>
D99 Diffuse Membranous CD99 in Ewing's
39 year old woman. Pain in the left leg. Left common perineal nerve sheath biopsy

Case 6
Some cells are adherent to delicate fibrovascular septa. Cells are epithelioid. Significant nuclear enlargement, prominent nucleoli, vesicular chromatin, appear rhabdoid
H&E

Dissociated high grade cells. Prominent melanoma like nucleoli
S100- Diffuse and Strong
DDx & Immunohistochemistry

- DDX: Carcinoma MPNST, Melanoma, Clear cell sarcoma, Epithelioid sarcoma, Epithelioid angiosarcoma
- AE1/3, EMA: Negative
- S100, SOX10: Positive
- HMB45, Melan A: Negative
- ERG, CD31: Negative
- INI-1: Lost
- TFE3: Negative
- Masson-Fontana: Negative
- Perls: Positive
- PAS: negative
Dx: MPNST, Epithelioid Variant

- No melanin pigment. An epithelipid MPNST. HMB45 and Melan A would be positive in epithelioid melanoma and clear cell sarcoma. Origin from a nerve.
Malignant Peripheral Nerve Sheath Tumor, Epithelioid Variant

- Uncommon variant, 5% of all MPNST. Epithelioid features have to dominate in MPNST to qualify for this dx
- Important to recognise: misdiagnosis as metastatic carcinoma or melanoma (1 or metastasis) and clear cell sarcoma
- Origin in a nerve in 80% cases. Difficult diagnosis otherwise
- Less common association with NF1 than usual MPNST
- Can arise after malignant transformation of schwannomas
- Diffuse and strong S100 positivity (unlike conventional spindled MPNST)
- Do not express melanoma (melanin) -associated antigens
- Keratin expression: rare
- Aggressive, 50% distant metastases
Further tumour, shows additional feature sometimes seen in epithelioid MPNST: myxoid change. Also rhabdoid cells - glassy eosinophilic cytoplasm - correlate of INI-1 (SMARCB1 loss)
54 year old male. Slowly enlarging left buttock mass. Tender.

Case 7
Unoriented piece of soft tissue 85x47x48. Haematoma cavity, congested fat. One 7mm white nodule seen near one pole of the specimen,
❖ Extensive zones of haemorrhage, Partial fibrous capsule, more cellular areas