Seminoma vs. Embryonal Carcinoma
Seminoma IHC

- Oct 3/4 positive.
- CD117 positive.
- CD30 negative.
- Typically keratin negative. However, occasionally scattered isolated loosely cohesive keratin positive cells that is still considered seminoma.

Seminoma vs. Large Cell Lymphoma
Pitfalls

- Although usually seminomas occur in younger men and lymphoma older, exceptions occur so can't rely on age and need to do IHC if morphology is not straightforward.

- OCT4 not as useful in this differential as rare lymphomas positive.

- Lymphomas are positive for CD45 and CD20, whereas seminomas are negative.

Germ Cell Tumor LVI vs. Artifactual Tumor in Vessels

Lymphovascular Invasion

Majority of studies show that lymphovascular invasion correlates with either lymph node metastases, or recurrence.

Most studies do not discriminate between lymphatic and venous/arterial invasion.
Staging of Germ Cell Tumors

- pT1 – Limited to testis (no LVI)
- pT2 – LVI or through tunica albuginea (rare)
  Involvement of hilar fat or epididymis (new criteria)
- pT3 – Spermatic cord involvement (at same plane as vas deferens)

Pitfalls in Identifying LVI

- Histiocytes in cord vessels.
- Best to look at periphery of tumor and in tunica albuginea.
Morphological Features of True LVI

- Tumor occupies a lymphovascular structure lined by flattened endothelial cells.

- The cluster will not conform to the exact shape of the vascular lumina.

- Associated fibrinous thrombosis and or mural attachment and re-endothelialization.

- Lack of obvious background artifactual deposition of germ cell tumor cells on the tunical surface.

- Cluster is more cohesive and has a rounded smooth edge.

- Cluster looks markedly different in its architecture from surrounding tumor.
Artifactual LVI
Syncytiotrophoblasts vs. Choriocarcinoma
Syncytiotrophoblasts

- Scattered cells most common in seminoma but can be seen in other GCTs
- Clustered around blood vessels, no cytotrophoblasts, no necrosis
- Serum HCG can be in 100s and when extensive in low 1000s
Choriocarcinoma

- Usually presents with symptoms due to widespread metastases
- HCG levels often >100,000
- Typically associated with advanced stage and poor prognosis but stage for stage comparable to other nonseminomatous germ cell tumors
Differential Diagnosis of Necrosis in the Testis

Different Types of Necrosis

- Coagulative – infarct with vasculitis (focal) or torsion (diffuse)
- Cellular – tumor
- Caseous - infectious

Necrotic Seminoma

Second to fourth decades, can be older.
Torsion

Any age but more common during childhood (two peaks: neonatal and adolescent).

Neonatal not associated with anatomical defect. Adolescent associated with bell-clapper abnormality.
Testicular Infarct

Most commonly 3rd to 4th decade but can affect older patients.

Isolated polyarthritis nodosum (PAN) like in most cases.

Granulomatous vasculitis more closely related to systemic vasculitis.

80% of men with PAN and 4% with Wegner granulomatosis have testicular involvement.
Infectious Necrosis

- Infections involving the testis always first involve the epididymis

- Granulomas with tuberculosis or fungi are discrete granulomas as opposed to the ill-defined granulomatous inflammation seen in about 25% of seminomas
Paratesticular Lipoma vs. Liposarcoma
Lipoma

- Typically located in the upper portion of the spermatic cord, although uncommonly seen at the distal cord.
- MDM2 negative
Liposarcoma

- Located at the base of the spermatic cord immediately adjacent to the testis. Average size 12 cm (3-30 cm).
- MDM2 overexpression yet not in every nucleus.
Dedifferentiated Liposarcoma

Most common high-grade dedifferentiated liposarcoma patterns are pleomorphic spindle or giant cell

Leiomyosarcomatous and osteoid differentiation may be seen

MDM2
Low-grade component resembling fibromatosis can be seen in dedifferentiated liposarcoma

Clear Cell Papillary vs. Clear Cell RCC & Papillary RCC
IHC, Treatment, Prognosis

- Distinctive CK7 and CAIX positive. CAIX membranous positive, yet not apically, resulting in cup-shaped pattern.
- Treatment: Partial or radical nephrectomy is curative.
- Prognosis: Vast majority stage T1 with excellent prognosis. No evidence of metastasis has been documented.

Clear Cell RCC
Clear Cell RCC with Area Mimicking Clear Cell Papillary RCC
Clear Cell Papillary RCC with Area Mimicking Clear Cell RCC

Papillary RCC
Angiomyolipoma
vs.
Normal Retroperitoneal Adipose Tissue
IHC, Treatment, Prognosis

- **IHC:** Spindle cell component positive for HMB45, Melan A, Cathepsin K. Smooth muscle actin and desmin often also positive. S100 can be positive.

- **Treatment:** Partial or radical nephrectomy or excision of retroperitoneal lesion.

- **Prognosis:** Benign although can involve lymph nodes. Can have significant morbidity and even mortality due to massive retroperitoneal hemorrhage.
Epithelioid AML with Atypia vs. High Grade RCC
**IHC & Prognosis**

- **IHC:** Typically positive for HMB45, Melan A, Cathepsin K. Cytokeratins and PAX8 negative.

- **Prognosis:** In one third of cases, recurrence and metastasis. Malignant behavior correlated with presence of 3 of the 4 following features: 1) >70% atypical epithelioid areas; 2) ≥2 mitoses per 10 HPF; 3) atypical mitotic figures; or 4) necrosis.
Oncocytoma vs. Chromophobe RCC

Prognosis and Reporting

- Oncocytoma – entirely benign. In report just state size and margins. Do not grade and do not comment if organ confined.

- Chromophobe RCC – With rare exceptions of high grade tumors, prognosis excellent with uncommon metastases. Do not grade as artifactually high.

CHROMOPHOBES RENAL CELL CARCINOMA IS A WELL-DEFINED VARIANT THAT HAS A SIGNIFICANTLY Better PROGNOSIS THAN CLEAR CELL CARCINOMA. WHILE CHROMOPHOBES RENAL CARCINOMAS ARE FREQUENTLY LARGE, TWO THIRDS OF THEM ARE CONFINED TO THE KIDNEY AT THE TIME OF DIAGNOSIS. WHILE MANY OF THESE TUMORS QUALIFY AS GRADE 3, THE GRADING SYSTEM DOES NOT ACCURATELY REFLECT THEIR PROGNOSIS. IN GENERAL, PATIENTS WITH STAGE PT1 AND PT2 CHROMOPHOBES TUMORS ARE ALMOST ALWAYS CURED BY SURGERY, WHILE PRESENTATION WITH PT3 OR PT4 DISEASE Is RARE. CONSEQUENTLY IT IS NOT RECOMMENDED TO ASSIGN A GRADE TO CHROMOPHOBES RENAL CELL CARCINOMAS.
Oncocytosis

- Numerous bilateral oncocytic nodules with oncocytomas, chromophobe RCCs, and hybrid tumors.
- Recommend nephron sparing surgery
- Some sporadic others with Birt Hogg Dube syndrome
  - Fibrofolliculomas
  - Pneumothorax
  - Other RCCs
IHC

• CK7 usually diffuse in chromophobe RCC and patchy in oncocytoma but some chromophobe RCCs are patchy.

• Hale's colloidal iron – typically not reliable

Papillary RCC with Oncocytic Features
Diagnosis of Oncocytoma on Needle Biopsy

- Some make definitive diagnosis

- I diagnose as: ONCOCYTIC NEOPLASM. SEE NOTE.

- NOTE: IF THIS BIOPSY IS REPRESENTATIVE OF THE ENTIRE LESION, IT WOULD BE CONSISTENT WITH AN ONCOCYTOMA. HOWEVER, RENAL CELL CARCINOMA MAY UNCOMMONLY SHOW FOCAL AREAS WITH ONCOCYTIC FEATURES.
Sarcomatoid RCC vs. Leiomyosarcoma
Sarcomatoid Carcinoma (Carcinosarcoma)

- Diagnose either by identifying keratin (HMWCK or pankeratin) in a tumor that would typically not express keratin

- Diagnose by identifying carcinoma elsewhere in the specimen (CIS or infiltrating UC in bladder; adenocarcinoma in prostate; RCC in kidney).