Testicular and Paratesticular Tumors Study Questions

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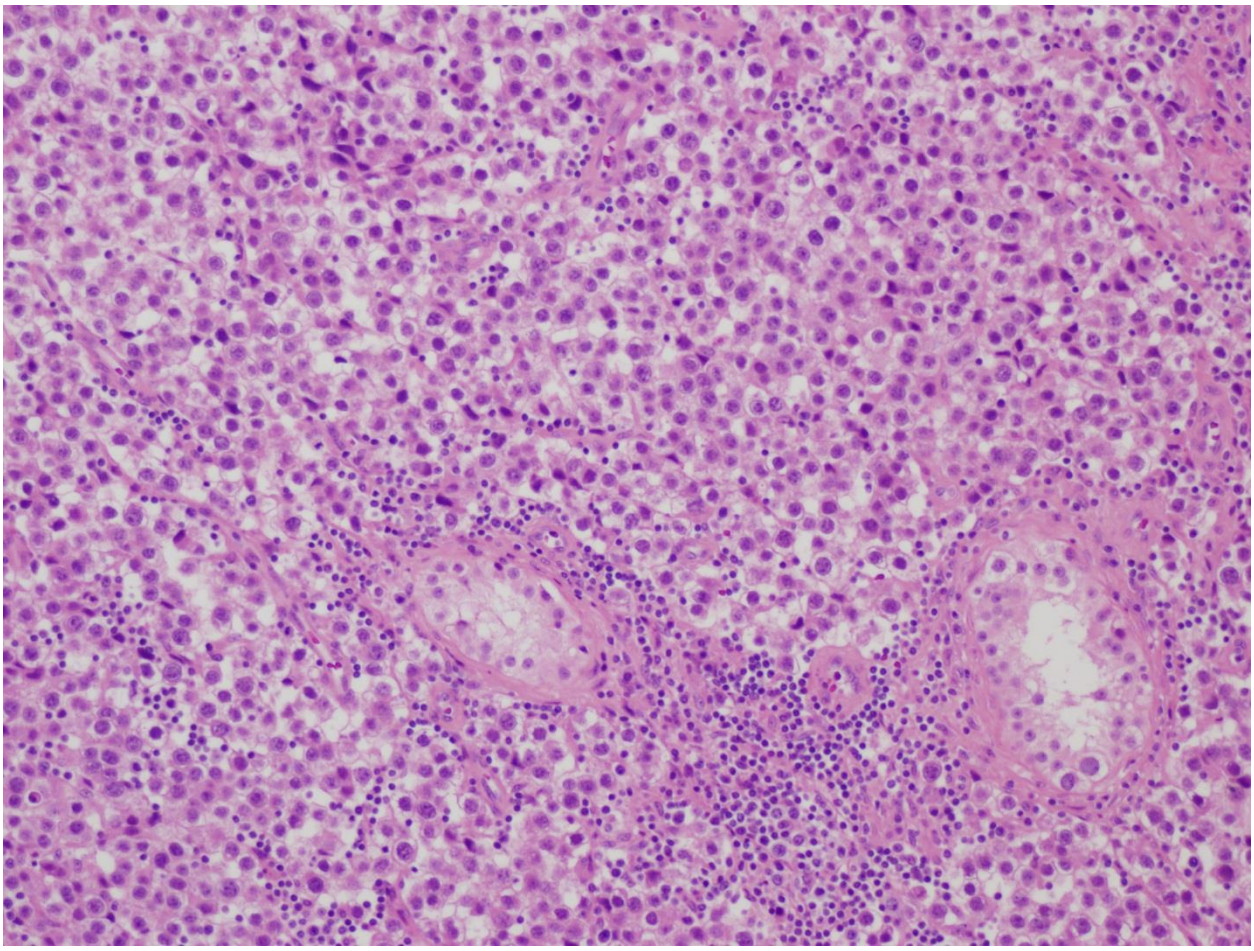
These questions correspond to the glass slide study set available in the Anatomic Pathology resident library. While photomicrographs are provided here with each question, *we strongly recommend review of the glass slides in order to fully benefit from each case*.

Thank you to Jacob S. Grange, M.D. for his contribution of many of the accompanying photomicrographs.

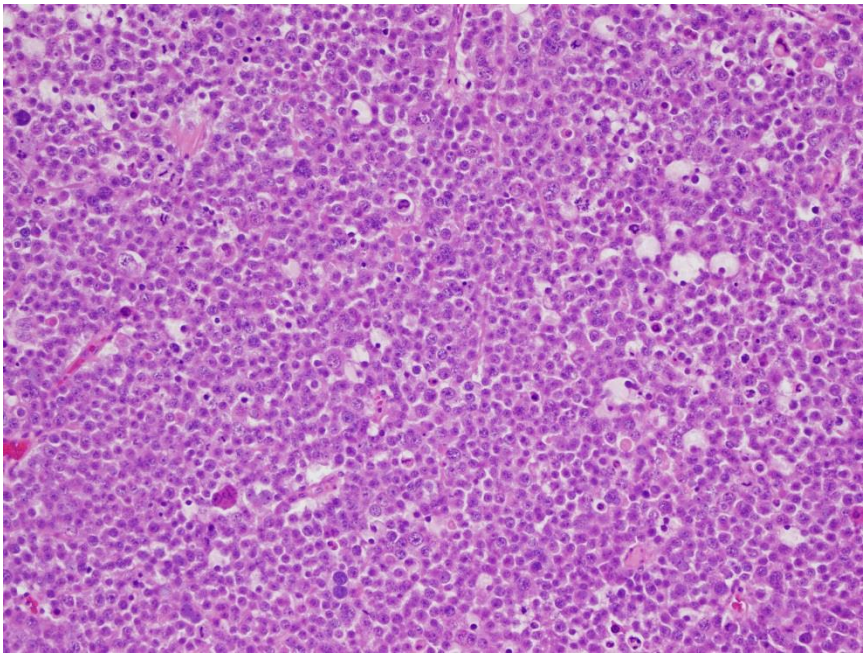
1. S13-1687

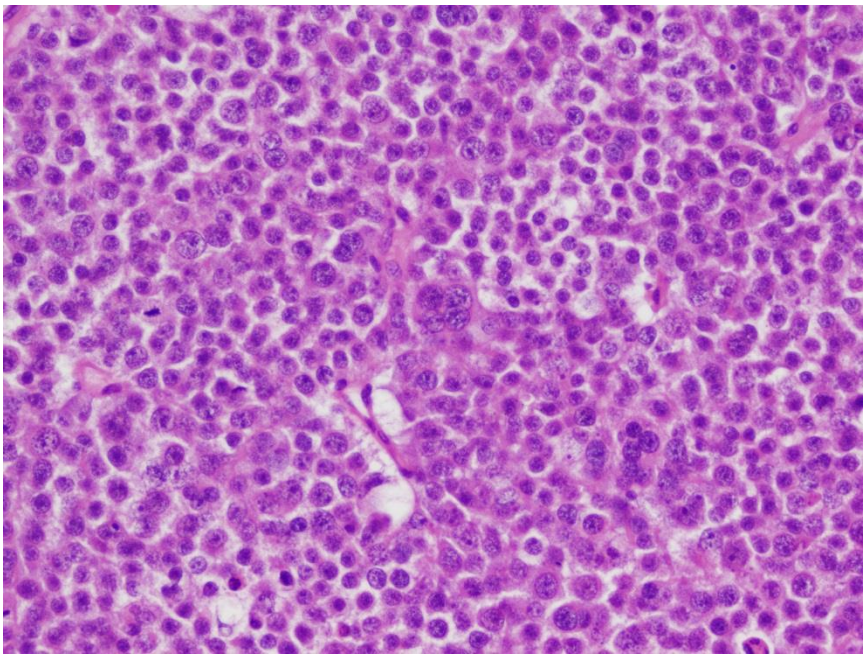


A 40-year-old man presents with a testicular mass. What is the expected immunohistochemical profile of this lesion?

A. SALL4 +, PLAP +, OCT3/4 +, CD117 -, CD30 +, AE1/AE3 +
B. SALL4 +, PLAP +, OCT3/4 +, CD117 +, CD30 -
C. SALL4 -, PLAP -, OCT3/4 -, CD117 -, CD30 -, inhibin +
D. SALL4 +, PLAP +, OCT3/4 -, CD117 -, CD30-, AFP +, AE1/AE3 +
E. SALL4 -, PLAP -, OCT3/4 -, CD117 -, CD30+, EMA +

2. CO16-2576

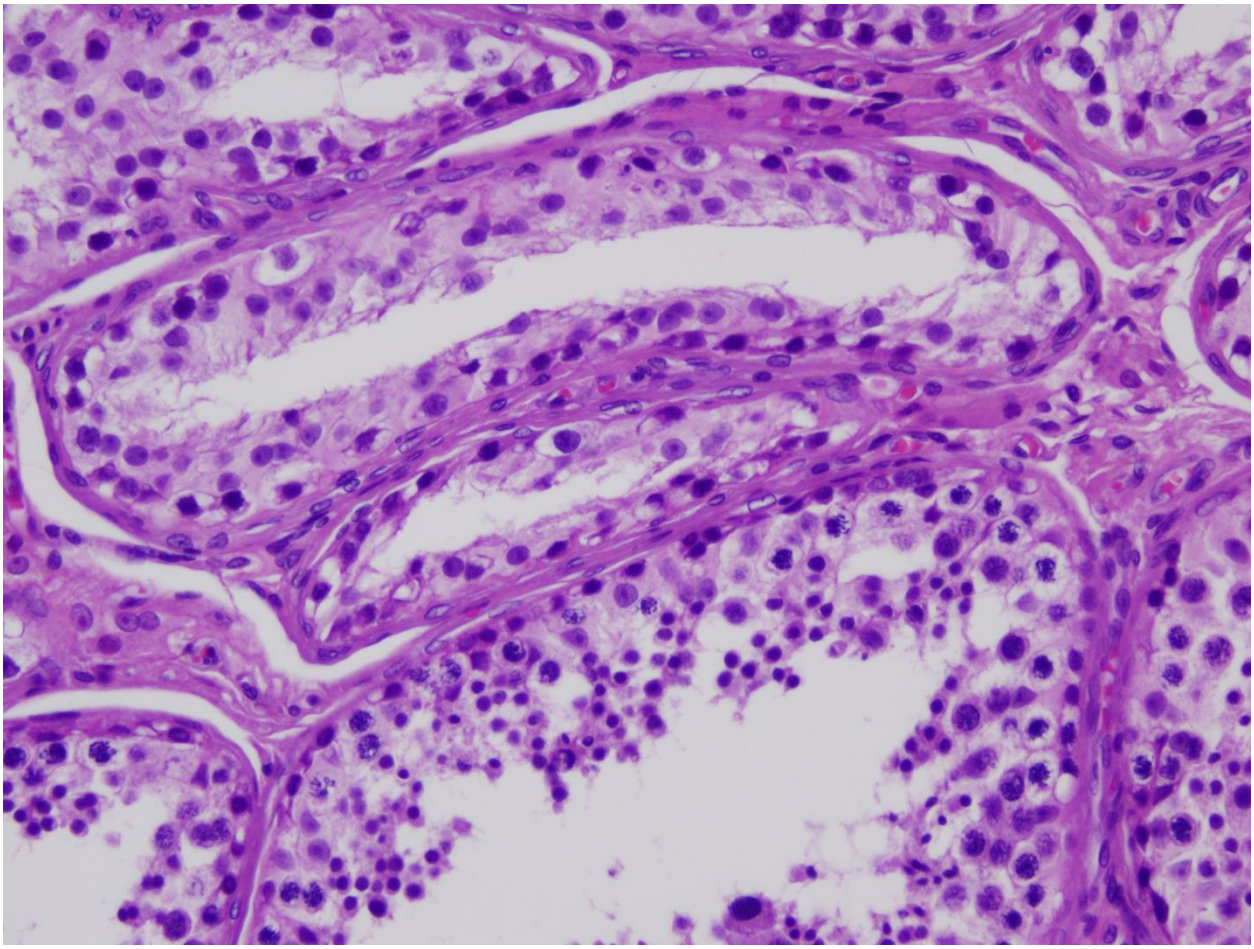




An 84-year-old man presents with a 4 cm testicular mass. On histologic examination, your differential diagnosis includes seminoma and spermatocytic tumor. In considering the differences between these two tumors, which feature would favor that this represents spermatocytic tumor?

A. Negative staining for CD117
B. Presence of intratubular germ cell neoplasia (IGCN)
C. Prominent associated granuloma formation
D. Presence of three cell types
E. Positive staining for OCT3/4

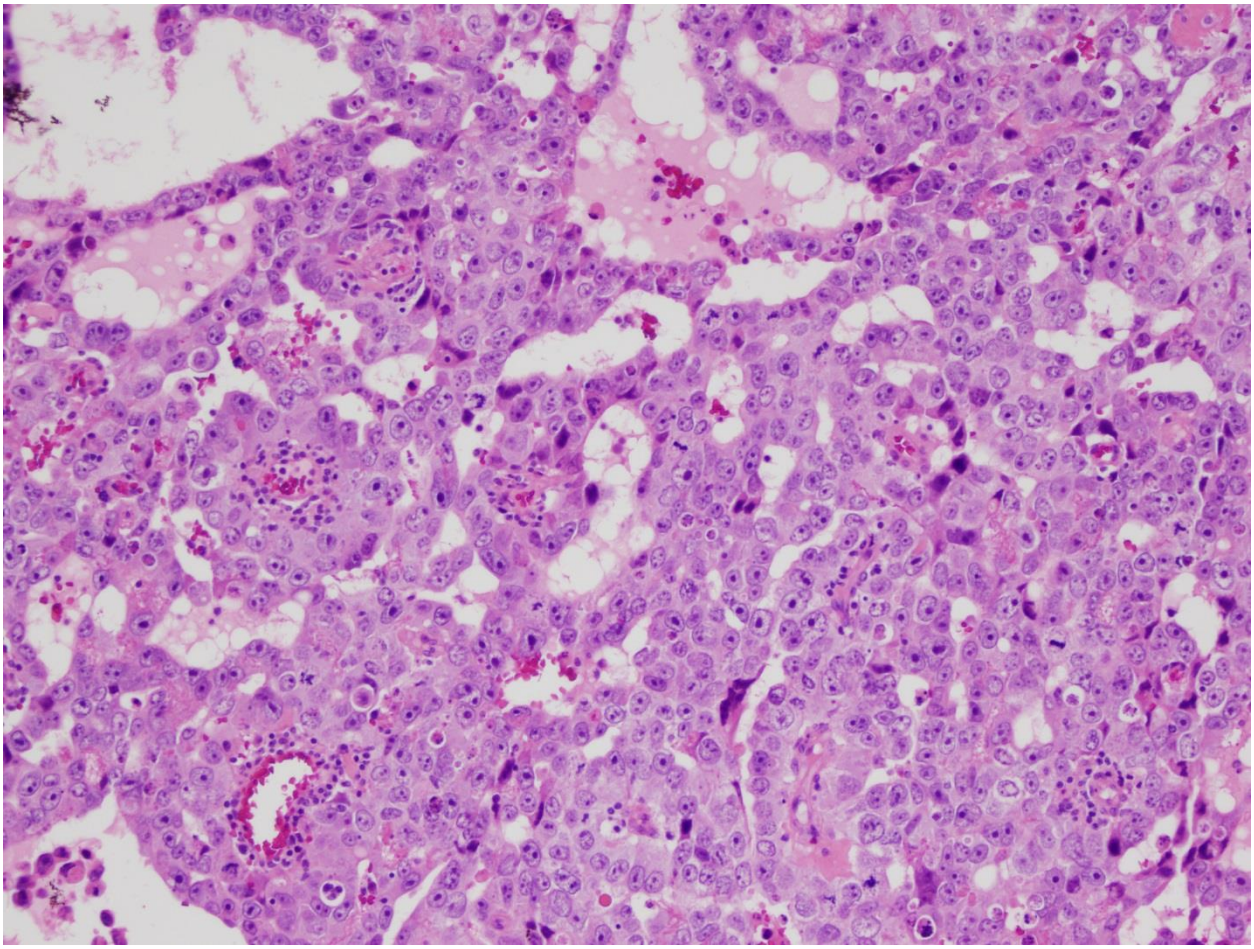
3. S05-28333



This is a testicular tumor from a 28-year-old man. Histologic examination demonstrates a mixed germ cell tumor (GCT). Adjacent to the primary tumor, the presumptive precursor lesion is seen (photomicrograph). Which of the following statements about testicular GCT precursor lesions is **false**?

A. Most adult germ cell tumors are thought to be derived from intratubular germ cell neoplasia, unclassified type (IGCNU), the invasive derivative of which appears to be seminoma.
B. IGCNU is not the precursor lesion to spermatocytic tumor.
C. Prepubertal forms of testicular germ cell tumors (yolk sac tumor and teratoma) are well documented to be associated with IGCNU, implicating it as the precursor lesion in these tumors.
D. Other forms of intratubular germ cell neoplasia exist, including intratubular embryonal carcinoma, intratubular trophoblast, and intratubular seminoma.
E. Due to its high sensitivity and specificity, OCT3/4 is the marker of choice for detection of IGCNU.

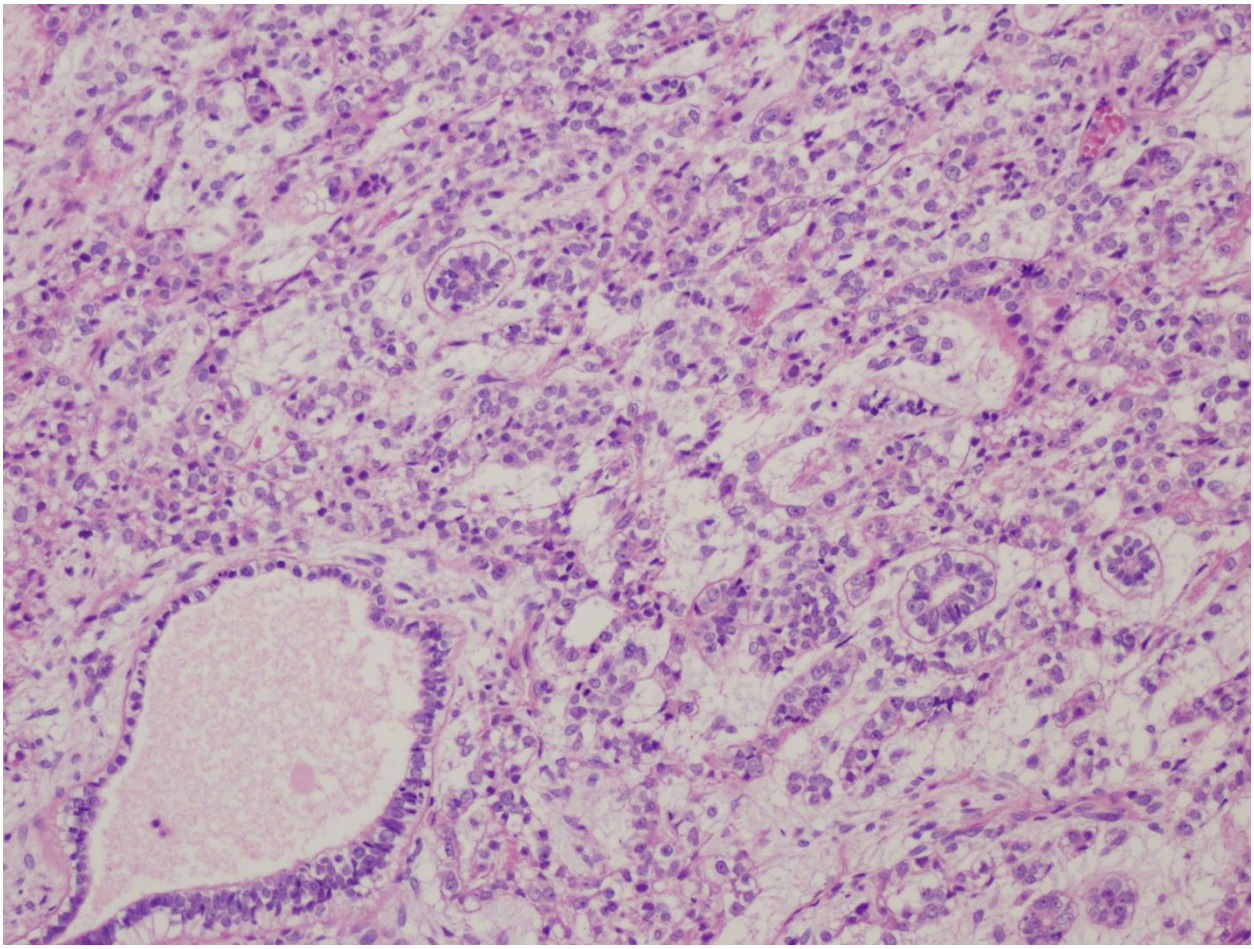
4. S13-7736



A 25-year-old man presents with a testicular mass. The orchiectomy specimen is well sampled and histologic examination demonstrates a mixed germ cell tumor (GCT) composed predominantly of embryonal carcinoma (photomicrograph) with a minor component of teratoma. In this setting, what additional finding would you expect?

A. Negative staining for OCT3/4 in the embryonal carcinoma component
B. Positive staining for CD117 in the embryonal carcinoma component
C. Markedly elevated serum AFP levels
D. Thyrotoxicosis as a presenting symptom
E. Isochromosome 12p or increased copy numbers of 12p on cytogenetic analysis of the tumor

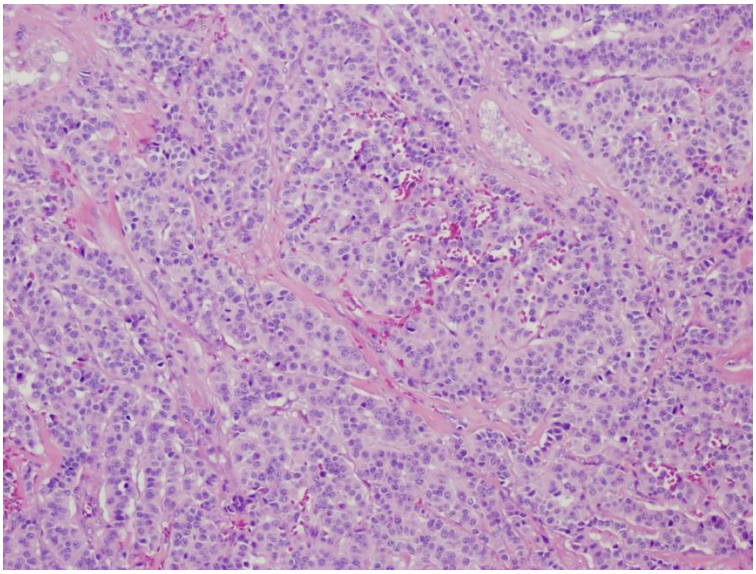
5. S13-26211

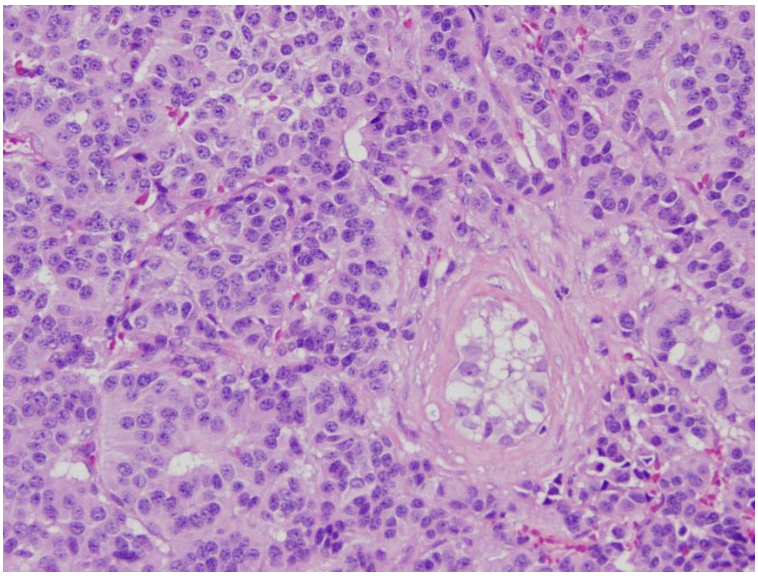


A 49-year-old man presents with a testicular mass. Histologic examination of the orchiectomy specimen demonstrates a mixed germ cell tumor (GCT) composed predominantly of yolk sac tumor (YST) (photomicrograph), with a minor component of teratoma. Which of the following statements about YST is **false**?

A. Hyaline globules are commonly present, and are a helpful clue in making the diagnosis.
B. Schiller-Duval bodies are pathognomonic, and are required to make a definitive diagnosis.
C. Glypican-3 is a more sensitive immunohistochemical marker than AFP in YSTs.
D. Elevated serum AFP level is seen in the majority of cases.
E. Pure YST is the most common form of testicular tumor in prepubertal children.

6. S09-21430

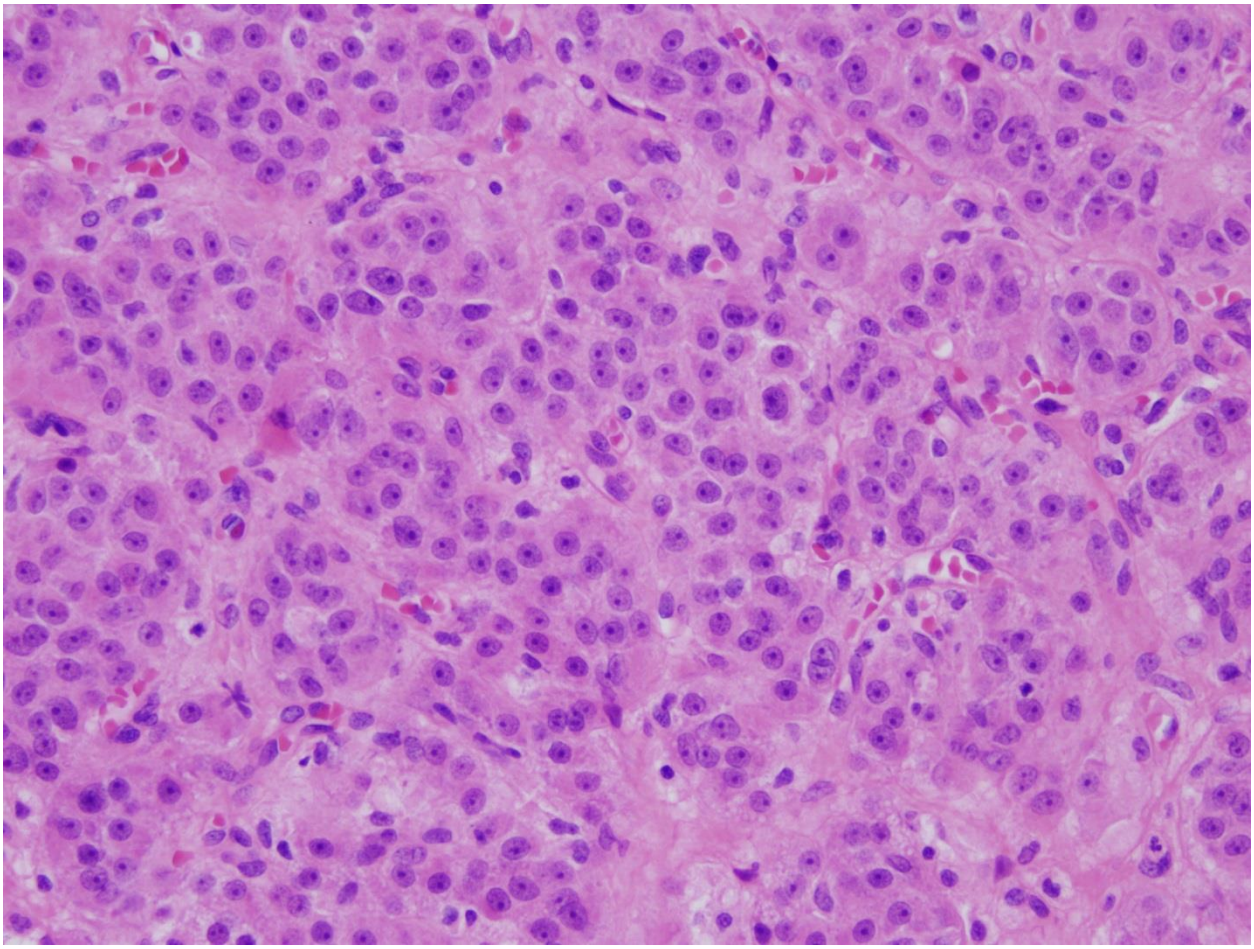




A 44-year-old man with no significant past medical history presents with a left testicular mass. Physical exam and radiographic studies show no evidence of any other masses. The patient undergoes an orchiectomy with thorough sampling of the lesion. Immunohistochemical staining demonstrates that the tumor is positive for pancytokeratin, chromogranin, synaptophysin, and CD56. Staining for AFP, PLAP, CD30, S-100, and inhibin are all negative. Which of the following statements is **false** regarding this tumor?

A. This tumor is considered to be a form of teratoma.
B. A minority of patients with this tumor present with clinical carcinoid syndrome.
C. This tumor frequently metastasizes and portends a poor prognosis. Adjuvant chemotherapy and radiation is therefore considered standard therapy.
D. Thorough and judicious sampling of this tumor should be performed in order to aid in the distinction between a primary versus a metastatic lesion.

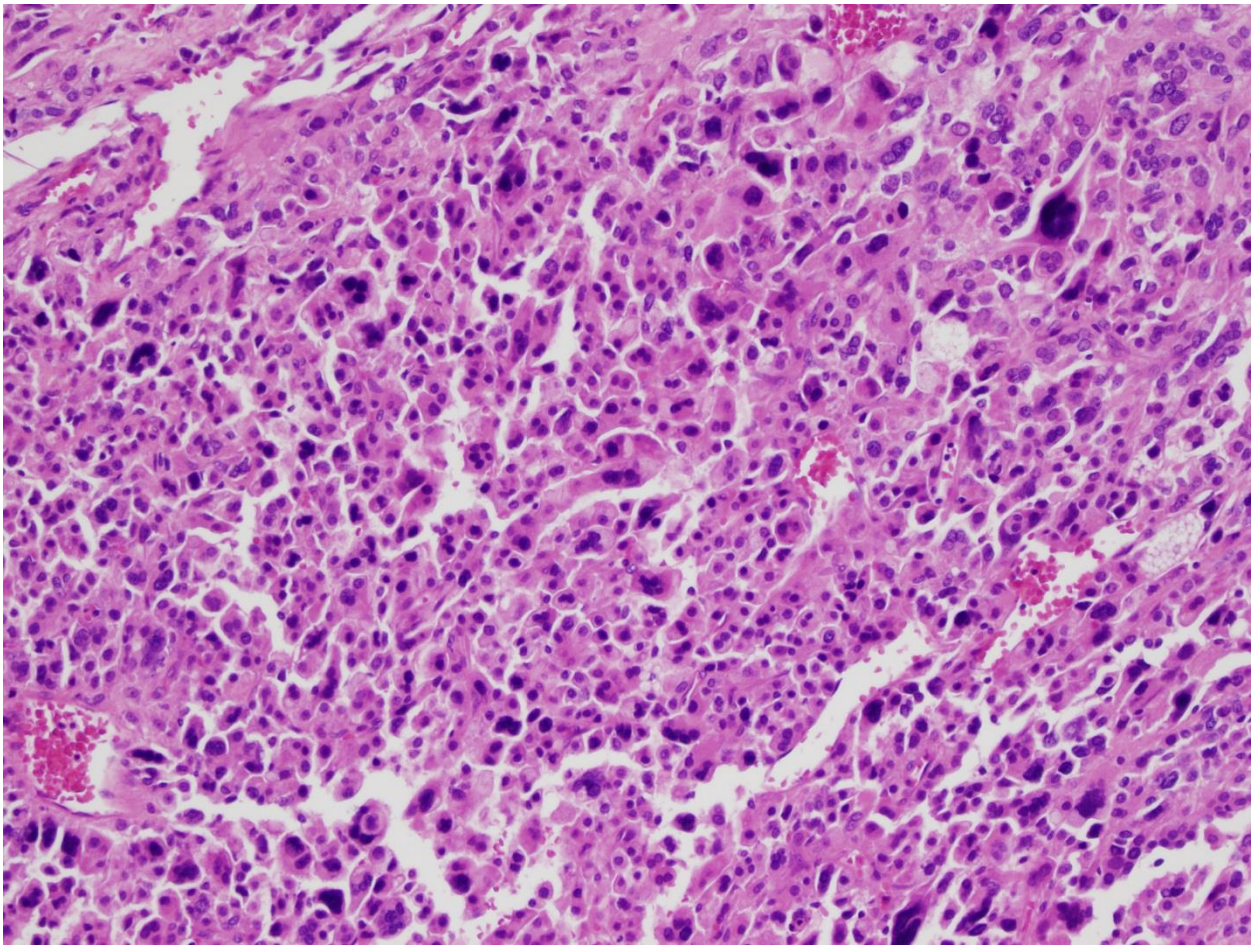
7. S13-28369



A 67-year-old man presents with a 1.2 cm right testicular mass. Gross examination demonstrated a well-circumscribed nodule with homogenous tan-yellow cut surfaces. Which immunohistochemical stain is expected to be **negative** in this tumor?

A. Calretinin
B. Inhibin
C. Melan-A
D. HMB-45
E. Vimentin

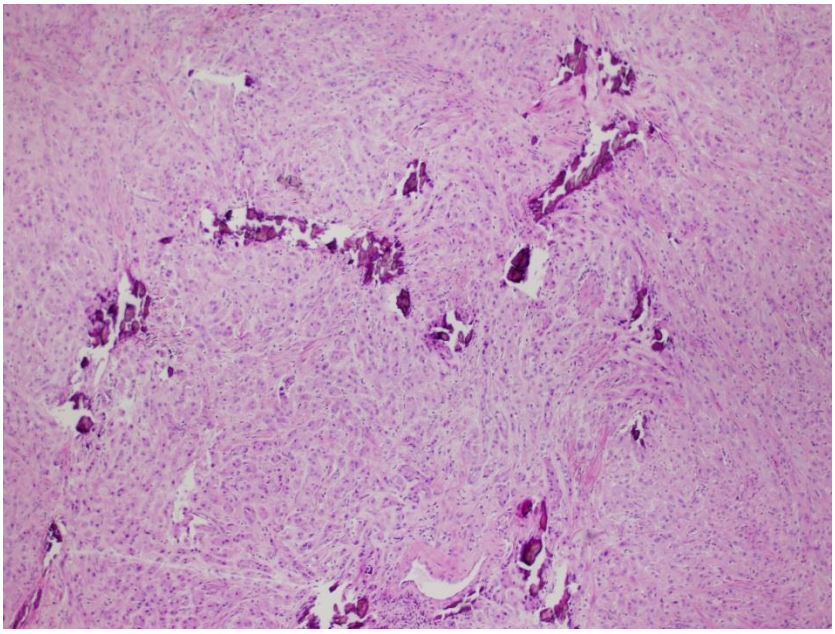
8. S16-24094

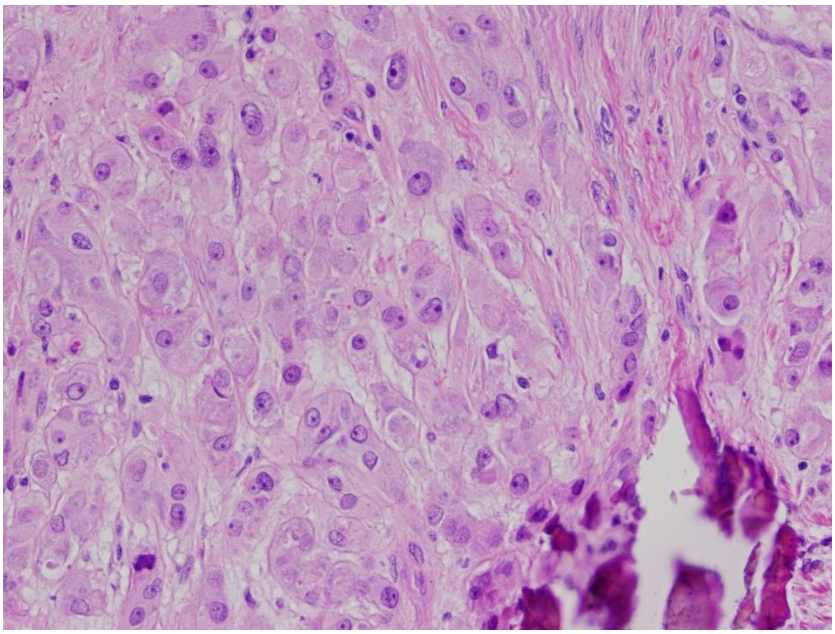


A 43-year-old man presents with a 9.8 cm right testicular mass. Which of the following features supports that this tumor is malignant?

A. Tumor diameter greater than 5 cm
B. Infiltrative borders
C. Cytologic atypia
D. Greater than 3 mitotic figures per 10 high-power fields
E. Vascular invasion
F. Necrosis
G. All of the above

9. CO16-900

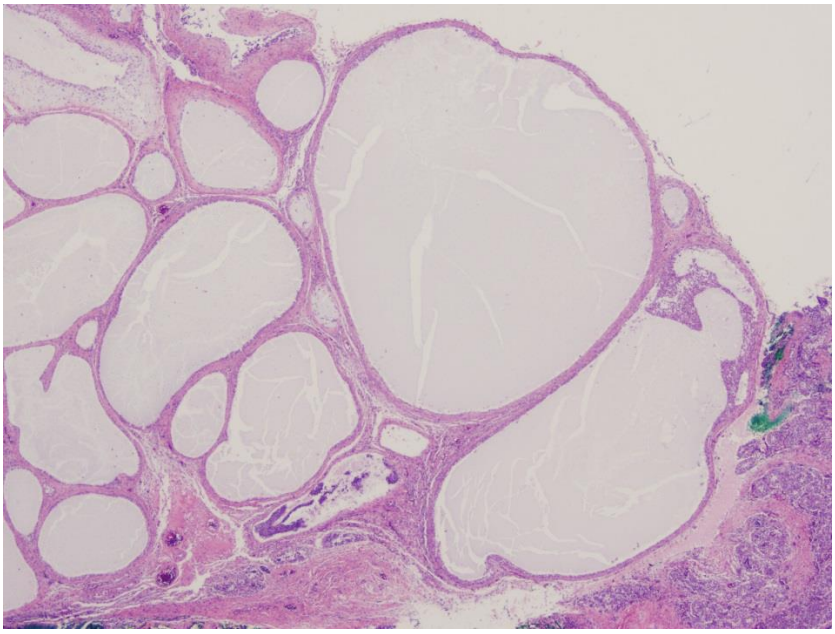


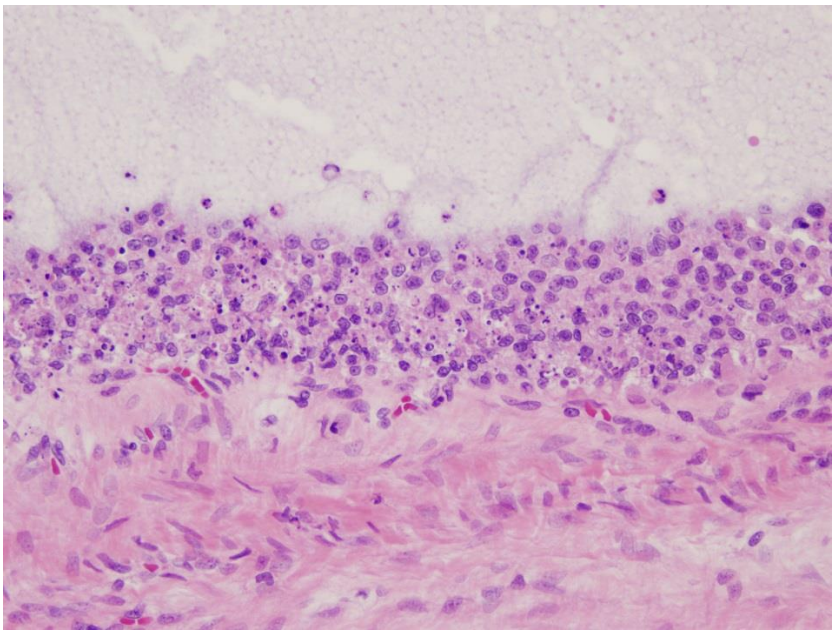


A 22-year-old man presents with a 2 cm right testicular mass. You review his prior surgical pathology specimen history and see he had a previous excision of a cutaneous myxoma. When preparing the report for the current orchiectomy specimen, you plan to mention the possibility of which syndrome in the diagnostic comment?

A. Carney complex
B. Carney triad
C. Mazabraud syndrome
D. Von Hippel-Lindau disease
E. Muir-Torre syndrome

10. S14-14710

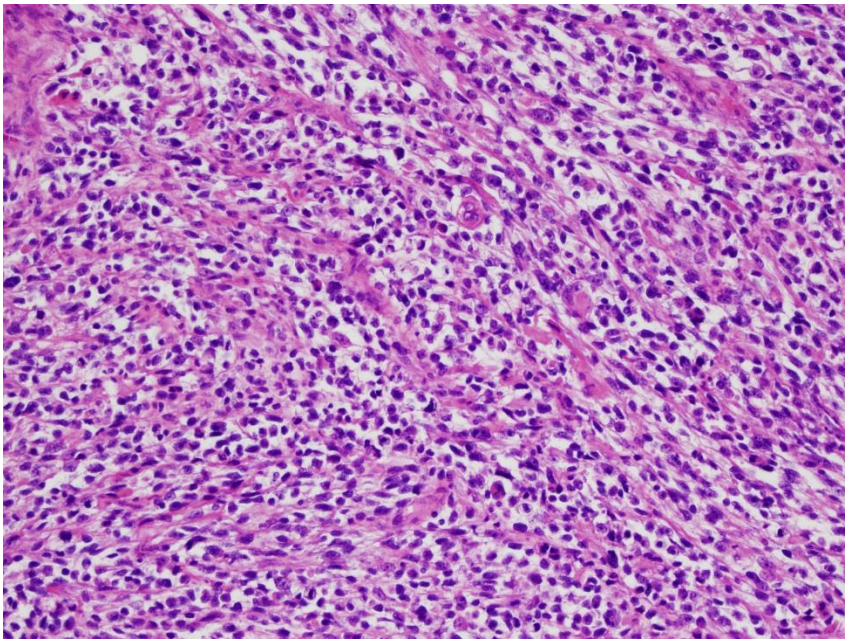


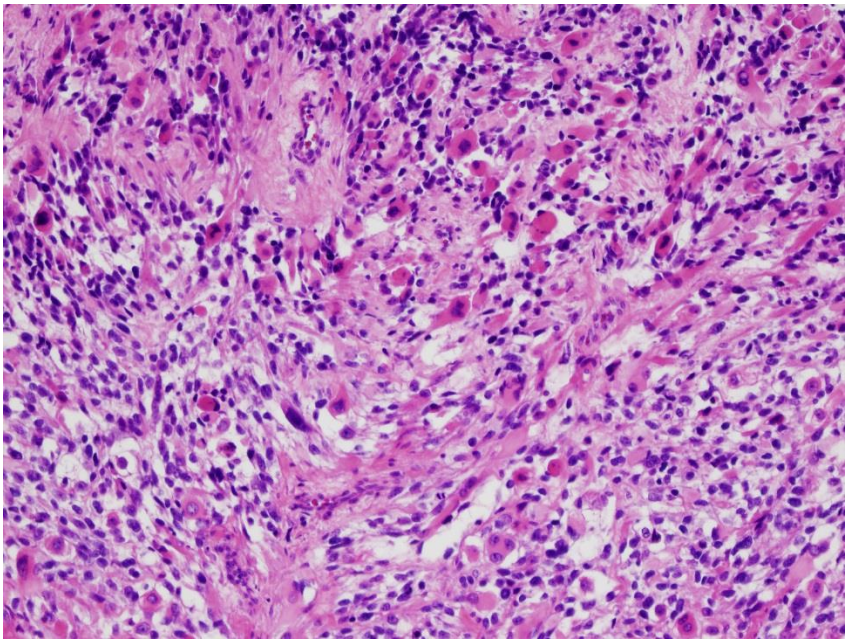


A 5-day-old male infant born at 40-weeks-gestational-age presents for evaluation of a 2 cm right testicular tumor noticed at birth. The tumor is noted to be predominantly cystic and filled with viscous fluid on gross examination. What is the diagnosis?

A. Teratoma
B. Epidermoid cyst
C. Dermoid cyst
D. Juvenile granulosa cell tumor
E. Yolk sac tumor

11. S17-6201

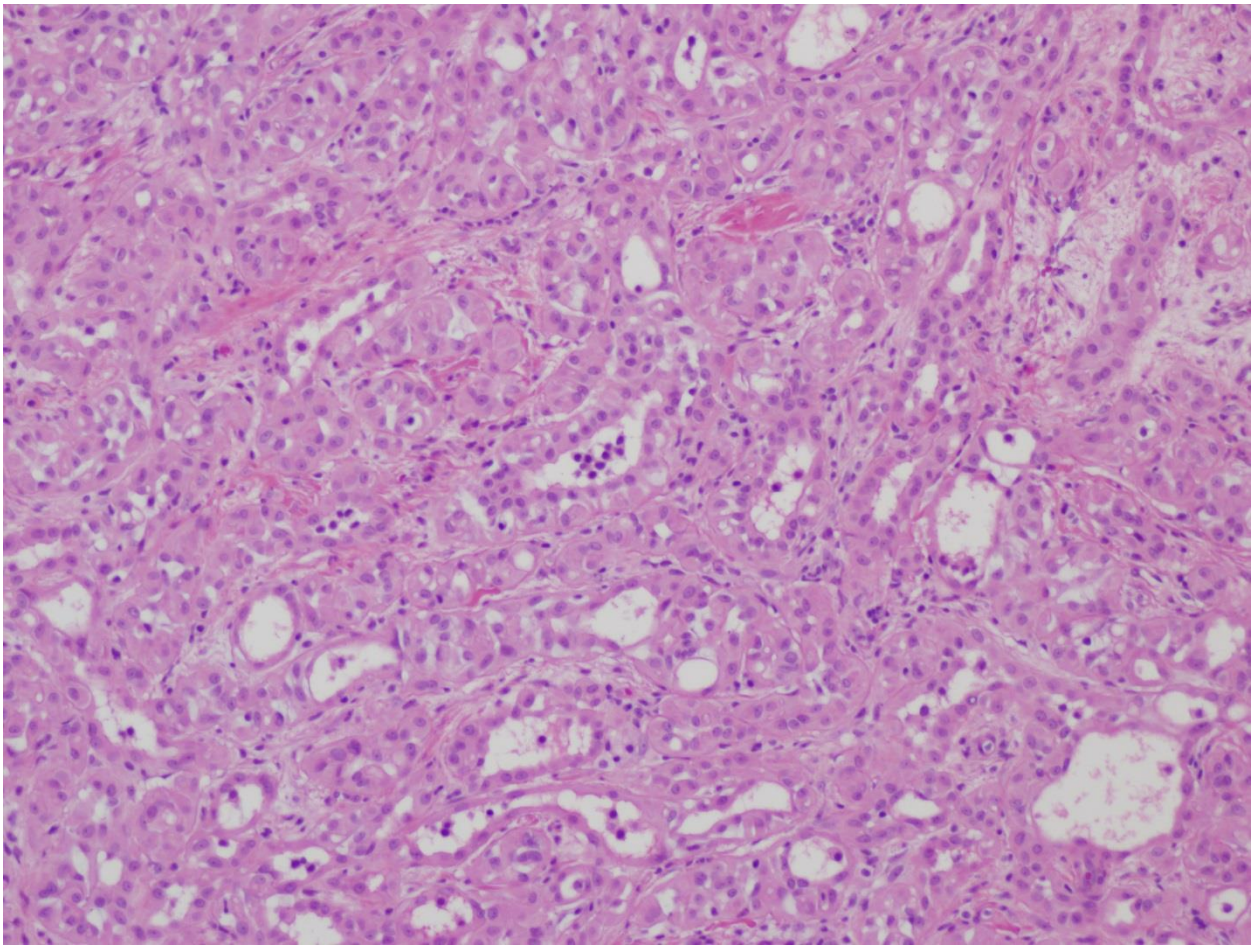




A 14-year-old boy presents with an 8.5 cm left paratesticular tumor. Which immunohistochemical profile would you expect in this tumor?

A. Myogenin (myf4) and MYOD1 positive
B. CD99 and FLI1 positive
C. CD45 and CD20 positive
D. Desmin and WT1 (C-19) positive
E. Vimentin positive and INI-1 negative

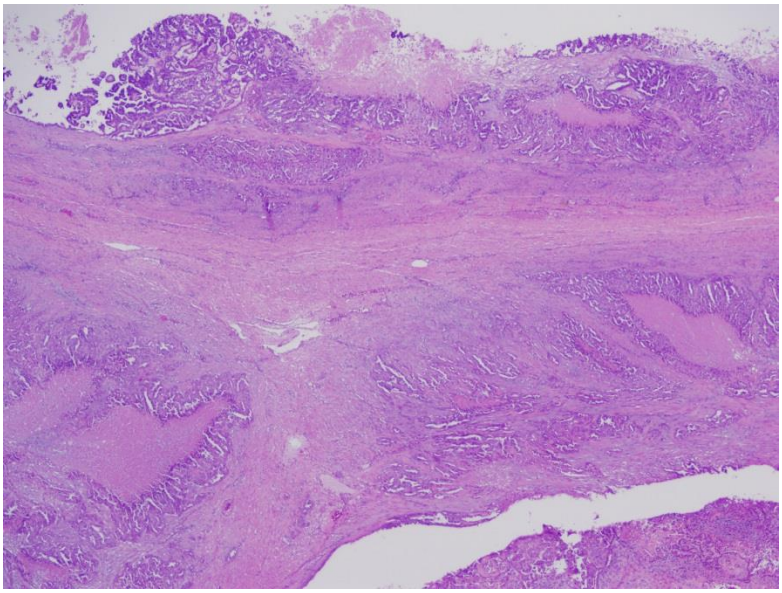
12. S12-23946:

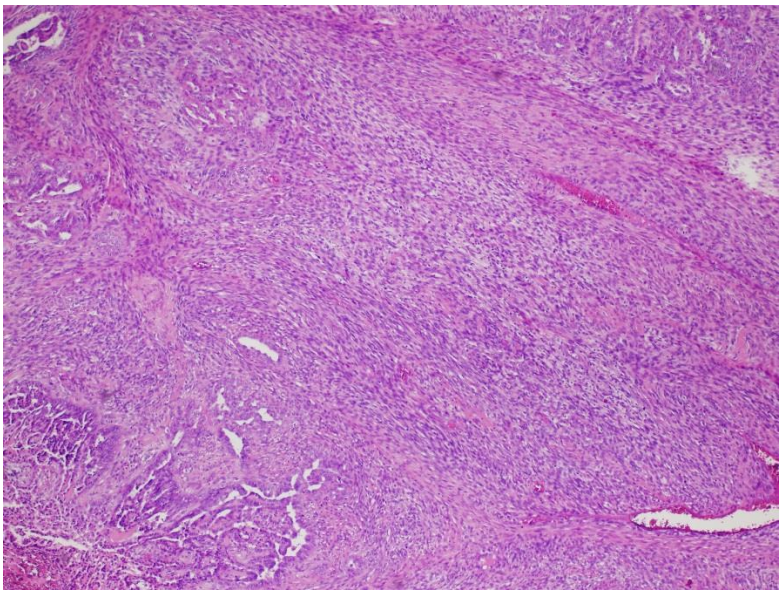


This is a 2.5 cm mass of the epididymis from 39-year-old man. Which immunohistochemical stain would you expect to be positive?

A. CD31
B. CD34
C. CEA
D. CK20
E. Calretinin

13. S05-13014

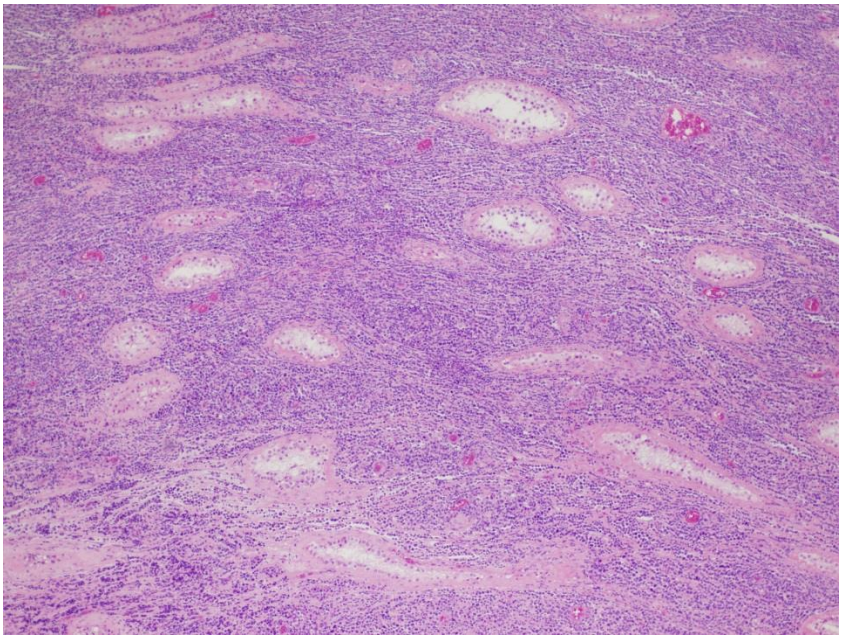


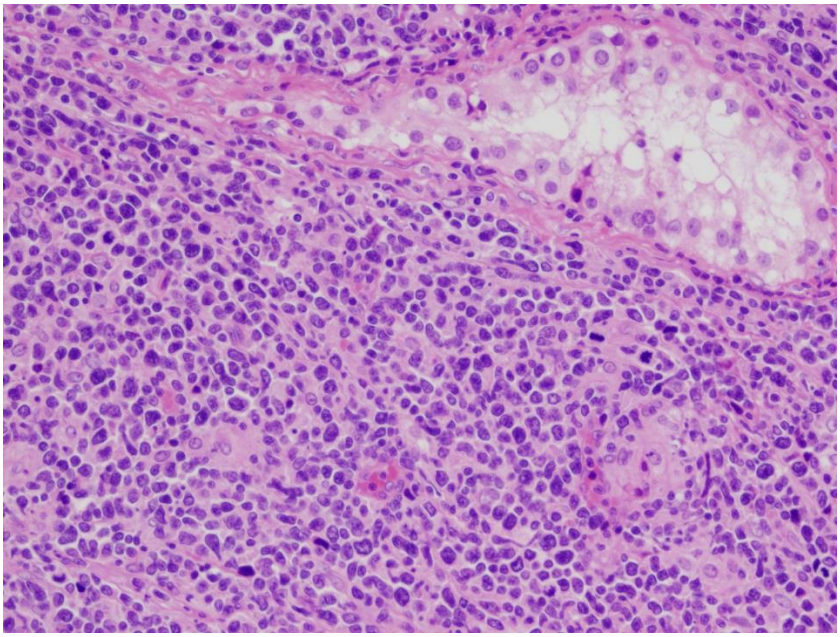


You are asked to review a case of paratesticular mass from a 61-year-old man who underwent a right orchiectomy. Review of the gross description reveals that the testicle was compressed by the wall of a 4.2 cm cystic area with variable thickness and distinct excrescences. Only a preliminary panel of immunohistochemical stains has been performed with the following results: pancytokeratin positive, EMA positive, BerEP4 weak focal positive. You base further work-up with which leading diagnosis in mind?

A. Epithelioid hemangioendothelioma
B. Epithelioid angiosarcoma
C. Epithelioid mesothelioma
D. Biphasic mesothelioma
E. Well-differentiated papillary mesothelioma

14. S17-2083

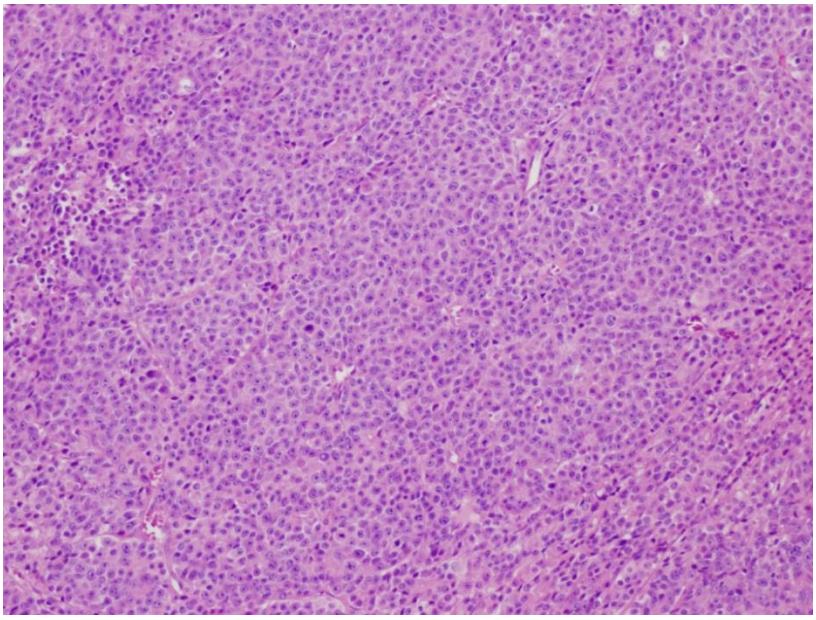


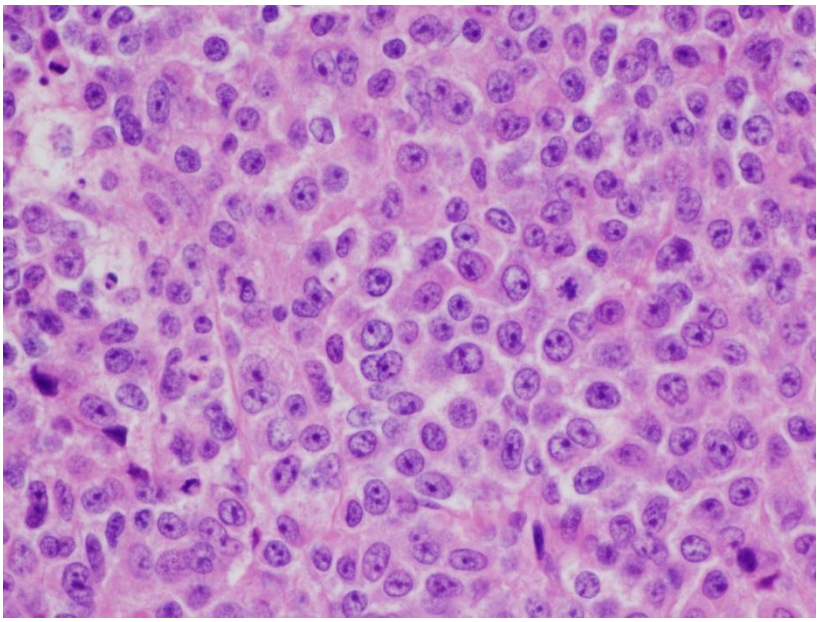


A 62-year-old man present with an 8 cm right testicular mass. A portion of the specimen is submitted for flow cytometric analysis which reveals a CD20 positive B lymphocyte population with the following phenotype: CD5 +, CD10 -, CD23 -, FMC7 +, kappa light chain restricted. What is the most likely diagnosis?

A. Chronic lymphocytic leukemia/small lymphocytic lymphoma
B. Mantle cell lymphoma
C. Diffuse large B cell lymphoma
D. Follicular lymphoma
E. Extranodal marginal zone lymphoma

15. S13-26348





An 83-year-old man presents with a 3.4 cm right testicular mass. You suspect this to be an embryonal carcinoma, but your initial panel of immunohistochemical stains demonstrates the following results: PLAP -, OCT3/4 -, CD30 -, AE1/AE3 +. After discussion with the surgeon, you learn the patient has a history of malignancy at another anatomic site. You therefore decide your second round of stains to include the following:

A. S100, Melan-A
B. CD45, CD20, CD3
C. PSA, PSAP
D. Hep-Par1, arginase-1
E. WT-1, calretinin

Answers

1. B

This is an example of a pure seminoma. Seminomas demonstrate positive staining for SALL4, PLAP, OCT3/4, and CD117 (c-kit). Seminoma is a malignant germ cell tumor (GCT), the cells of which are considered the neoplastic counterparts of the primordial germ cells during early embryonic development. It is the most common testicular germ cell neoplasm, accounting for 50% of all GCTs. Mean age at presentation is 37-41 years. Histologically the tumor is composed of a diffuse arrangement of pale cells with crisp cytoplasmic membranes and intervening fibrovascular septa containing lymphocytes. It is important to differentiate pure seminomas from nonseminomatous germ cell tumors, as low stage pure seminomas portend an excellent prognosis. Patients with stage I disease who are treated with adjuvant radiation or single-agent chemotherapy achieve a 95-98% 5-year survival rate.

Answer A is the immunoprofile for embryonal carcinoma, answer C for sex cord stromal tumors, answer D for yolk sac tumor, and answer E is often seen in anaplastic large cell lymphoma.

2. D

This is an example of a spermatocytic tumor (spermatocytic seminoma). Spermatocytic tumor accounts for approximately 1% of testicular germ cell tumors (GCT) and is thought to be derived from postpubertal germ cells, commonly spermatogonia or early primary spermatocytes. This tumor occurs at a mean patient age of 52-59 years, a considerably older age than is associated with GCTs derived from intratubular germ cell neoplasia (IGCN), which is absent in spermatocytic tumor. Tumors are usually 3-5 cm, are lobular to multinodular with gray-white, hemorrhagic, fleshy, or myxoid cut surfaces.

On microscopic examination, tumor cells are arranged in diffuse to multinodular patterns that are often interrupted by edema, which can impart a pseudoglandular appearance when fluid accumulates centrally within nests. The hallmark histologic feature however is a polymorphous population of tumor cells composed of three cell types: small cells with round, uniformly dense nuclei and scant cytoplasm; intermediate-sized cells with round nuclei with finely granular to filamentous chromatin and variably prominent nucleoli; and giant cells with single or multiple nuclei bearing nuclear features similar to those of the intermediate-sized cells. The intermediate-sized and giant cells typically display dense eosinophilic to amphophilic cytoplasm. Mitotic activity and apoptotic bodies are easily identified.

In contrast to the histologic features of seminoma, spermatocytic tumor displays poorly defined cytoplasmic membranes, scanty intervening stroma, sparse to absent lymphocytic infiltrates, and only rare granulomas.

Spermatocytic tumors stain negatively for many of the markers for embryonic germ cell tumors including OCT3/4, PLAP, AFP, beta-HCG, and CD30. Positive staining is seen with proteins expressed in spermatogonia including SALL4, MAGEA4, and CD117 (c-kit). CD117 positivity is also seen in seminomas.

These tumors portend an excellent prognosis, and have rarely, if ever, been documented to metastasize, unless there is an associated component of sarcomatous dedifferentiation. When present, the sarcoma component is entirely undifferentiated or may display rhabdomyosarcomatous, angiosarcomatous, or other forms of differentiation. Hematogenous dissemination occurs in approximately 50% of cases with sarcoma and prognosis is poor.

3. C

This is an example of a mixed testicular adult germ cell tumor (GCT) composed of embryonal carcinoma and teratoma. Intratubular germ cell neoplasia, unclassified type (IGCNU) is seen adjacent to the invasive tumor. Under the current model of testicular GCT pathogenesis, the cells of IGCNU are a proliferation of intratubular germ cells that have undergone malignant transformation. These cells eventually develop into invasive tumor, in the form of seminoma, based on morphologic, immunohistochemical, ultrastructural, and genetic studies. This supports that seminoma is a common precursor to several other forms of invasive germ cell tumors.

Other forms of IGCN are recognized, including intratubular embryonal carcinoma, intratubular trophoblast, and intratubular seminoma. Intratubular embryonal carcinoma is always seen in association with IGCNU, suggesting an alternative pathway to the development of nonseminomatous tumors. Intratubular trophoblast has also been identified in seminomas in which trophoblastic giant cells are present. Intratubular seminoma likely represents an end stage of IGCNU, prior to the development of invasive tumor.

This proposed model of testicular GCT neoplasia does not apply to spermatocytic tumor, prepubertal testicular GCTs (yolk sac tumor and teratoma), or to specific types of adult teratomas (dermoid and epidermoid cysts). Its association with prepubertal testicular GCTs is debated, with some studies claiming an absence of associated IGCNU, while other dispute its absence.

Immunohistochemistry for OCT3/4 is considered a highly sensitive and specific marker for IGCNU, and furthermore demonstrates easily interpretable nuclear reactivity, making it an ideal marker for the assessment of the presence of this lesion.

4. E

Embryonal carcinoma (EC) is composed of tumor cells which resemble embryonic stem cells with ovoid to columnar cells with clear to granular cytoplasm and markedly pleomorphic nuclei with vesicular chromatin and macronucleoli. Mitotic figures, including atypical mitotic figures and apoptotic bodies are easily identified. Several architectural patterns may be observed including solid, glandular, papillary, nested, micropapillary, anastomosing, pseudopapillary, sieve-like glandular, and blastocyst-like. Of these patterns, solid, glandular, and papillary are most common. After seminoma, EC is the most prevalent GCT of the testis. While 2-16% of GCTs are pure ECs, EC occurs in 40% of all GCTs and in 87% of nonseminomatous GCTs. The most useful immunohistochemical stains for distinguishing EC from other GCTs are positivity for CD30 and OCT3/4. CD30 is most helpful in that it selectively stains EC, but expression may be lost post-chemotherapy. Isochromosome 12p and increased copy numbers of 12p have been demonstrated in the majority of ECs, a finding which can distinguish it from other non-germ cell poorly differentiated malignancies.

Positive staining for CD117 is seen in seminoma. Elevated serum AFP level is seen in yolk sac tumors. Thyrotoxicosis can be a presenting symptom of choriocarcinoma. This is thought to be due to the cross-reactivity of beta-hCG with thyroid-stimulating hormone (TSH).

5. B

Adult YST is a malignant GCT which resembles extraembryonic structures, including the yolk sac, allantois, and extraembryonic mesenchyme. Most patients present with a painless testicular mass, are 15-40 years old, and have elevated serum AFP levels (98% of cases). There are 11 histologic patterns of YST, typically occurring in combination. In order of decreasing prevalence: microcystic/reticular, myxomatous, macrocystic, solid, glandular/alveolar, endodermal sinus/perivascular, hepatoid, papillary, sarcomatoid/spindle cell, parietal, and polyvesicular vitelline. Two features commonly seen in many patterns include the presence of intracytoplasmic and extracellular hyaline globules and irregular band-like intercellular deposits of basement membrane, called parietal differentiation. The hyaline globules are round, eosinophilic, PAS-positive, diastase-resistant and typically range in size from 1 to 50 microns in diameter. Schiller-Duval (glomeruloid) bodies are structures composed of connective tissue cores containing a single central vessel with a peripheral mantle of tumor cells and are seen in the less common endodermal sinus/perivascular pattern. Approximately 80% of YSTs demonstrate cytoplasmic immunoreactivity for AFP, which may be focal. Glypican-3 is a more sensitive marker, with positivity seen in nearly 100% of cases. Pure YST is the most common form of testicular tumor in prepubertal children (median age of presentation 16 to 20 months), and in this setting portends a good prognosis with an overall 5-year survival rate of 90%.

6. C

This is an example of a primary testicular carcinoid tumor. This tumor is considered to be a monodermal teratoma. While most testicular carcinoids are pure neoplasms, they can be seen associated with other teratomatous elements. Mean age of presentation is 46 years, although they can occur in the second to ninth decades. Clinical carcinoid syndrome is encountered in approximately 10% of cases.

Histologic examination reveals solid islands, occasionally forming small acini, composed of cells with round nuclei with granular chromatin and eosinophilic cytoplasm. Immunohistochemical staining for markers of neuroendocrine differentiation are positive (chromogranin, synaptophysin, CD56). It is important to distinguish primary testicular carcinoids from metastatic carcinoid tumors. If seen, the presence of teratomatous elements supports a primary testicular tumor and therefore careful sampling of the lesion is warranted. Metastatic carcinoids are often bilateral and multifocal and frequently show lymphovascular invasion. Additionally, patients will have evidence of tumor at extratesticular sites.

The prognosis of primary testicular carcinoid tumor is good, although metastases have been reported. Malignant behavior is associated with patients who present with carcinoid syndrome, or whose tumors are greater than 7 cm. Therapy consists of orchiectomy with clinical follow up.

7. D

This is an example of a Leydig cell tumor. Leydig cell tumors are the most common type of testicular sex cord-stromal tumor and represent approximately 2% of all testicular neoplasms. These tumors occur over a wide age range, but most commonly occur in the third to sixth decades. Children with these tumors can present with isosexual pseudoprecocity due to the androgenic hormone production of the tumor. Both adult and pediatric patients may present with gynecomastia because of aromatase-mediated conversion of androgens to estrogens.

Histologic examination demonstrates a tumor composed of polygonal cells with eosinophilic cytoplasm, which is occasionally clear or vacuolated. The nuclei are round a display a central prominent nucleolus. Architecturally, the tumor is usually arranged in a diffuse sheetlike pattern, although nests, ribbons, and cords within fibrous stroma may be observed. Lipofuscin is present in the cytoplasm in approximately 15% of cases, and intracytoplasmic Reinke crystals are seen in approximately 30% of cases. Leydig cell tumors stain positively for inhibin, calretinin, melan-A, and vimentin, and may show patchy reactivity with low-molecular weight cytokeratins. HMB-45 positivity is not a feature of Leydig cell tumors.

8. G

This is an example of a malignant Leydig cell tumor. Approximately 5% of Leydig cell tumors are clinically malignant, although their behavior is not always predictable. Features that help predict malignancy are tumor diameter greater than 5 cm, infiltrative borders, cytologic atypia, greater than 3 mitotic figures per 10 high-power fields, vascular invasion, and necrosis. Increased Ki-67 index labelling greater than 5% and p53 overexpression can also be used to aid in the assessment of malignancy. Patients with malignant Leydig cell tumors will often undergo retroperitoneal lymph node dissection for staging purposes. Radiation and chemotherapy are usually not effective and recurrences can develop after several years.

9. A

This is an example of a large cell calcifying Sertoli cell tumor (LCCSCT). LCCSCT is a rare neoplasm that can occur either in association with Carney complex or sporadically. Germline mutations of the PRKAR1A gene on chromosome 17q are found in about 60-70% of Carney complex-associated cases. This gene is believed to function as a tumor suppressor gene. This tumor is often seen in teenage boys to young adults, and those that are associated with Carney complex are usually identified after other features of the disorder identify an at-risk patient. Carney complex-associated cases are typically bilateral and multifocal, while sporadic cases are nearly always unilateral and unifocal.

Tumors range in size from less than 1 to 15 cm. Cut surfaces are tan to white, lobulated, and have a gritty texture. Microscopically, the tumors is composed of solid tubules, nests, clusters, and cords of cells with abundant, somewhat granular eosinophilic cytoplasm, occasionally within a fibromyxoid stroma with neutrophils. Nuclei are round or oval with small to intermediate-sized nucleoli. Calcifications may be small and psammomatous to prominent and plaque-like. Immunohistochemical staining for inhibin and S100 are positive, while (unlike other Sertoli cells tumors) nuclear beta-catenin is negative. Although uncommon, having two of the following features correlates with malignant behavior: size greater than 4 cm, greater than 3 mitoses per 10 high-power fields, nuclear atypia, necrosis, lymphovascular space invasion, and extratesticular growth.

Carney complex (or Carney syndrome) is an autosomal dominant disorder characterized by predisposition to myxoid lesions (cardiac myxoma, skin angiomyxoma, myxoid fibroadenoma of the breast), pigmented and calcifying lesions (spotty skin pigmentation, epithelioid blue nevus, pigmented nodular adrenocortical hyperplasia, psammomatous melanotic schwannoma, LCCSCT), and endocrine hyperactivity (pituitary adenoma, chondroid hamartoma).

LCCSCT may also be seen in association with Peutz-Jeghers syndrome.

10. D

This is an example of a testicular juvenile granulosa cell tumor. This tumor is most commonly found in infants less than 5 months of age, and a proportion of them are congenital. On gross examination, these tumors are well-circumscribed and display an admixture of solid and cystic foci filled with viscous fluid. Histologic examination reveals variably sized follicles filled with fluid and intervening fibromuscular stroma. The follicles are lined by several layers of cells with pale to eosinophilic cytoplasm and hyperchromatic round nuclei with small nucleoli. Mitotic figures are usually readily identified. Inhibin, calretinin, vimentin, and CD99 are positive, while cytokeratin, SMA, and desmin are only occasionally positive. This tumor follows a benign course.

Yolk sac tumor and teratoma are the two most common testicular germ cell tumors in the prepubertal period. Prepubertal yolk sac tumor has a median age of presentation of 16-20 months. Epidermoid and dermoid cysts are considered specialized forms of testicular teratoma. Epidermoid cysts typically present in the second to fourth decades and are composed of stratified squamous epithelial lining without skin appendages. Dermoid cysts are considered a specialized variant of prepubertal teratoma composed of a stratified squamous epithelial lining with associated apocrine and eccrine sweat glands in a collagenous stroma, similar to the dermis.

11. A

This is an example of embryonal rhabdomyosarcoma. This tumor consists of sheets of poorly to moderately differentiated cells with a round morphology and eccentrically placed oval nuclei. The cytoplasm may be scant, and is granular and deeply eosinophilic. As cells become larger, the cytoplasm may become more fibrillar. In about half of these tumors, cells with cross-striations in the cytoplasm are observed. Occasionally, the characteristic strap cell may be seen, in the form of spindle cells with cytoplasmic borders that run in parallel without tapering. When such cells are present, the lesion is considered to be well differentiated. The background stroma is often loose and myxoid. The most useful immunohistochemical stains are myogenin (myf4), MYOD1, desmin, and muscle-specific actin. Myoglobin is less sensitive, but highly specific.

Distinct histologic subtypes of embryonal rhabdomyosarcoma include botryoid and spindle cell. The spindle cell variant of embryonal rhabdomyosarcoma is the most common malignant tumor of the paratesticular region in childhood and has a much better prognosis than other subtypes of embryonal rhabdomyosarcoma. Other variants, including alveolar and pleomorphic are less common at this site.

Therapy for paratesticular rhabdomyosarcoma includes orchiectomy with retroperitoneal lymph node dissection with combination of chemotherapy and radiation therapy. The overall survival rate is approximately 80%, while the spindle cell variant has a much better outcome and is associated with a lower rate of lymph node metastases. The alveolar subtype may not portend a worse prognosis, as in other sites, perhaps due to more intensive therapy.

CD99 and FLI1 positivity are seen in Ewing sarcoma; CD45 and CD20 in B cell lymphoma; desmin and WT1 (C-19) in desmoplastic small round cell tumor; and vimentin positive, INI-1 negative in rhabdoid tumors.

12. E

This is an example of an adenomatoid tumor. Adenomatoid tumor is a benign mesothelial neoplasm and is the second most common neoplasm of the paratesticular region (after spermatic cord lipoma). While this tumor can occur across a wide age range, mean age of presentation is 36 years. The tail of the epididymis is the most common site, but they can occur anywhere in the epididymis. Less commonly, they occur in the spermatic cord, tunica albuginea, or tunic vaginalis. Grossly, these lesions are well-circumscribed and display homogeneous white-tan bulging cut surfaces. Typically they are less than 2 cm, but can be up to 5 cm. Histologically, this tumor is composed of gland-like or vascular-like spaces lined by vacuolated or attenuated cells that often form thin, bridging strands across the lumen. Additionally, the tumor may be composed of epithelioid cells with abundant granular eosinophilic cytoplasm may be seen growing in chains or solid clusters. The background stroma is collagenous, often hyalinized, with occasional admixed smooth muscle. These tumors stain positively for pancytokeratin, CK7, and mesothelial markers calretinin, WT1, HBME1, and podoplanin. Cytokeratin 20, epithelial markers (CEA, BerEP4, B72.3) and endothelial markers (CD31, CD34) are typically negative.

13. D

This is an example of biphasic mesothelioma. This case shows a predominantly papillary architecture composed of epithelioid cells with vesicular chromatin, prominent nucleoli, and brisk mitotic activity. There is a second component composed of sheets of malignant spindle cells with indistinct cell borders, and vacuolated cytoplasm. There is associated zones of geographic necrosis.

Mesotheliomas of the paratesticular tissue arise from the tunica vaginalis, which forms the double layer of mesothelium that lines the outer surface of the tunica albuginea and inner layer of the scrotum. Mean age of presentation is 60 years. While mesotheliomas of other sites are strongly associated with asbestos exposure, the association at this site is less robust; approximately 30-40% of cases of paratesticular mesothelioma have been reported to be associated with prior asbestos exposure. Grossly, these tumors appear as a thickening of the tunica vaginalis forming papillary masses enveloping, and often invading, the testicular parenchyma.

Mesotheliomas can show several different histologic patterns. Those that occur at this site tend to be epithelioid with papillary or tubulopapillary architecture. Only 25% show mixed epithelioid and sarcomatoid pattern (biphasic pattern), while purely sarcomatoid pattern is quite rare. The cells may be bland and resemble normal mesothelium, or may demonstrate marked pleomorphism with mitotic activity and prominent nucleoli. The immunohistochemical profile for mesotheliomas at this site is similar to those of the pleura with positive staining for calretinin, WT1, thrombomodulin, and EMA; however, CK5/6 may show only patchy positivity. BerEP4 can show weak focal positivity.

Treatment involves radical orchiectomy, retroperitoneal lymph node dissection, chemotherapy, and radiation. Recurrences tend to occur within 1-2 years of follow-up.

14. B

Lymphoma arising in the testis accounts for 5% of all testicular neoplasms and is the most common testicular neoplasm in men older than 50 years, making it an important diagnostic consideration when evaluating any testicular lesion. While *secondary* involvement of the testis by lymphoma is a more common scenario (as was the case in this patient), the vast majority of *primary* testicular lymphomas in adults are diffuse large B cell lymphomas.

Gross examination demonstrates a fleshy white-tan to pink neoplasm, sometimes with extratesticular involvement. Scanning magnification will usually disclose an interstitial growth pattern, with relative tubular preservation, although this is not specific to lymphoma.

Regarding primary testicular lymphomas, stage is an extremely important prognostic indicator, as true testicular primaries limited to the testis (stage IE) have a 5-year survival of 60%, compared to 17% for all other stages.

This particular case is an example of mantle cell lymphoma (MCL) secondarily involving the testis. MCL is a B cell lymphoma composed of small cleaved lymphocytes, characterized by the t(11;14) translocation involving cyclin D1 and immunoglobulin heavy chain genes resulting in the expression of cyclin D1. The neoplastic cells are usually CD5 +, CD10 -, CD23 -, FMC7 +, CD43 +, Bcl-2 +, and Bcl-6 -. Paraimmunoblasts and centroblasts should be absent. Clinically important aggressive variants are composed of cells that resemble lymphoblasts (blastoid variant) or cells that resemble diffuse large B cell lymphoma (pleomorphic variant). MCL is usually disseminated at diagnosis, and is among the most aggressive non-Hodgkin lymphomas, with a 5-year survival rate of 27%. This case is composed of atypical lymphoid cells with marked pleomorphism and increased mitotic activity, consistent with transformation to a blastoid or pleomorphic variant.

15. C

This is an example of metastatic prostatic adenocarcinoma to the testis. Prostatic adenocarcinoma is the most common metastatic malignancy to the testis, accounting for approximately 33% of metastases to this site.

Metastases to the testis frequently occur in patients with a known history of malignancy, and are consequently often easily recognizable. However, the pathologic recognition of a testicular metastasis may be challenging when the testicular mass is the presenting feature of an occult malignancy or relevant clinical history is not provided to the pathologist. In a review of adults with metastases to the testis, more than two-thirds of cases were primaries from prostate, gastrointestinal tract, kidney, and lung.

On microscopic examination of these lesions, there are particular diagnostic pitfalls that may befall the unsuspecting pathologist. Metastatic renal cell carcinoma, clear-cell type is prone to be misinterpreted as Sertoli cell tumor. Metastatic melanoma can display cytoplasm that resembles that of Leydig cell tumors, or grow as discohesive cells between tubules, mimicking lymphoma. Metastatic prostate cancers can sometimes display growth in the rete testis or within the seminiferous tubules, leading to interpretation of rete testis carcinoma or seminoma, respectively.

Other (albeit less robust) clues to the diagnosis of a metastatic lesion include older age (mean age 57) than patients who present with germ cell tumors, multinodular growth pattern on gross examination, bilateral testicular involvement (present in 10-20% of cases), intertubular growth pattern, extensive lymphovascular space invasion, and absence of intratubular germ cell neoplasia (IGCN).

Answers A and B are incorrect in the setting of positive staining for cytokeratin AE1/AE3. The morphologic features seen in this case of sheets of cells with prominent nucleoli make answers D and E less likely. While not specific, prominent nucleoli are commonly seen in prostatic adenocarcinoma. Hepatocellular carcinoma and mesothelioma only rarely metastasize to the testis, accounting for 0.4% and 0.2% of metastases to this site, respectively.

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