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Adult Non-Germ Cell Tumors of the Testis and Scrotum

Learning Objective: At the conclusion of this continuing medical education activity, the participant will be able to define the presentation, evaluation and treatment of prominent benign and malignant non-germ cell tumors seen in clinical practice.

This AUA Update aligns with the American Board of Urology Module on Oncology, Urinary Diversion and Adrenal. Additional information on this topic can be found in the AUA Core Curriculum section on Oncology–Testis.

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INTRODUCTION

Germ cell tumor of the testis is the most common testicular pathological entity. **Therefore, all suspicious testicular masses should be evaluated by physical examination, imaging and serum tumor markers (STMs).** However, practicing urologists should be familiar with benign and malignant non-germ cell testicular masses for a thorough evaluation of the patient. It is important to be knowledgeable about the evaluation, treatment and pathological characteristics of these tumors since management can differ from the more common germ cell tumors (see table). This Update presents the different management strategies for adult non-germ cell tumors of the testis and scrotum.

BENIGN TESTICULAR/PARATESTICULAR LESIONS

Benign testicular lesions are typically found incidentally and follow an indolent course. In clinically confusing scenarios, surgical management can be diagnostic and therapeutic.

Epidermoid and dermoid cysts. Patients with testicular epidermoid and dermoid cysts most commonly present with a painless testicular mass. These cysts are now considered a subtype of prepubertal-type teratoma. These tumors are considered benign and comprise 14% of childhood and 2% of adult testicular neoplasms.[1,2] **Ultrasound (US) of the testicle often reveals the classic "onion ring" like laminated appearance (fig. 1).** Figure 2 demonstrates on hematoxylin & eosin staining the keratinized debris produced within a unilocular cystic mass that is common with these tumors. Epidermoid cysts differ from dermoid cysts in that they lack adnexal structures. Testicular dermoid cysts are a rare benign variant of cystic teratoma analogous to what is seen in the ovary. While they share the similar findings of the presence of diverse tissue types with postpubertal teratomas (ie intestinal mucosa, cartilage and bone), they lack the cytological atypia seen in postpubertal teratomas and by definition are not associated with germ cell neoplasia in situ.[3] Unlike mature teratomas, epidermoid cysts lack isochromosome 12p and 12p overrepresentation, so fluorescence in situ hybridization analysis can be utilized in challenging diagnostic cases.[4] In very rare cases, primary carcinoid tumors have been associated with both epidermoid and dermoid cysts. However, they have a benign clinical course, unlike primary atypical carcinoid tumors, which can exhibit metastatic spread.[5]

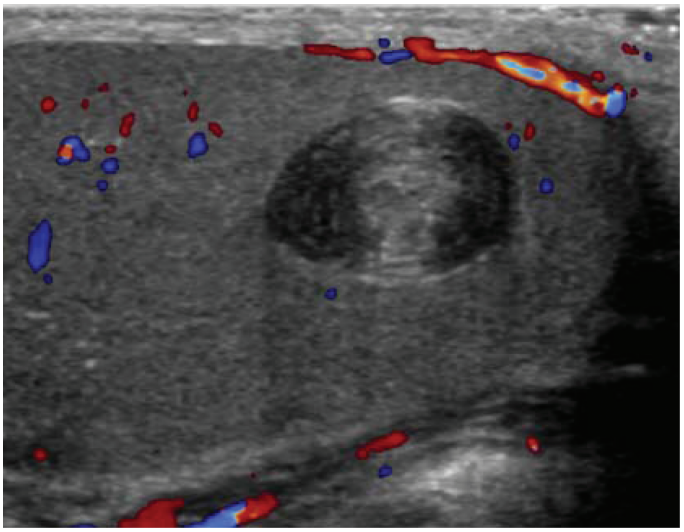

Figure 1. Ultrasound image of epidermoid cyst. Note classic "onion skin" appearance without Doppler signal. Reprinted with permission from Kern SQ, Speir RS, Akgul M et al: Rare benign and malignant testicular lesions: histopathology and management. Curr Opin Urol 2020; **30:** 235.

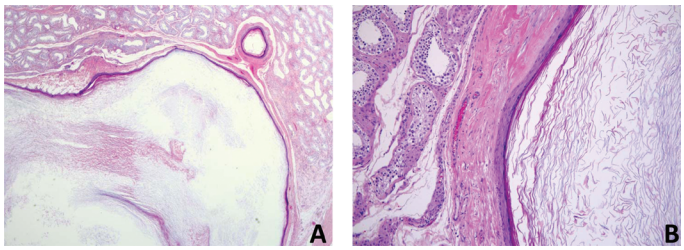

Figure 2. Epidermoid cyst of testis. Recently recognized as subtype of prepubertal-type teratoma, these lesions are not associated with germ cell neoplasia in situ or isochromosome 12p, and are invariably benign. Well-circumscribed cysts lined by squamous epithelium contain concentric keratin debris. Cyst wall does not include adnexal structures such as hair follicles. *A*, H&E, reduced from ×20. *B*, H&E, reduced from ×100. Reprinted with permission from Kern SQ, Speir RS, Akgul M et al: Rare benign and malignant testicular lesions: histopathology and management. Curr Opin Urol 2020; **30:** 235.

Evaluation and management of epidermoid and dermoid cysts are similar. Analysis of STMs is prudent, along with imaging studies. **Once normal tumor markers are confirmed and the US imaging reveals an "onion ring" like appearance, inguinal incision with temporary occlusion of the spermatic cord followed by partial testis-sparing orchiectomy or enucleation appears to be a reasonable and safe management option.**[6,7] For patients not amenable to surgical management, surveillance can be considered when classic characteristics are present.

Adenomatoid tumors. Adenomatoid tumors are responsible for 30% of paratesticular masses and 1%–2% of testis masses.[8,9] These tumors are usually asymptomatic and slow growing, and present as a painless scrotal mass. The tumors typically present in patients during the third and fourth decades of life; however, finding them in patients over 70 years of age has been described.[10] Evaluation and management involve obtaining STMs and imaging. **Pathological diagnosis of any intratesticular**

ABBREVIATIONS: CAH=congenital adrenal hyperplasia, CNS=central nervous system, CT=computerized tomography, DHEA=dehydroepiandrosterone, LCT=Leydig cell tumor, MRI=magnetic resonance imaging, OS=overall survival, PET=positron emission tomography, R-CHOP=rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone, RFS=recurrence-free survival, RMS=rhabdomyosarcoma, RP=retroperitoneal, RPLND=retroperitoneal lymph node dissection, RT=radiation therapy, SCT=Sertoli cell tumor, STM=serum tumor marker, TSS=testis-sparing surgery

vascular mass on imaging is recommended. Excisional biopsy is both diagnostic and therapeutic. Testis-sparing surgery (TSS) is increasingly being evaluated in tumors that have a benign appearance or are isolated and non-palpable on imaging. In the setting of small testicular masses less than 2.8 cm^3 and negative tumor markers, Paffenholz et al suggest consideration of TSS as this can accurately differentiate between benign and malignant disease, with an 83% sensitivity and 89% specificity for predicting malignancy.[9] **The decision regarding TSS vs radical orchiectomy for small tumors should be made through a shared decision-making process between the patient and physician after discussion of the oncologic and surgical risks and benefits.**

TESTICULAR SEX CORD STROMAL TUMORS

Tumors of the testis that arise from non-germinal epithelium are classified as sex cord stromal tumors. They comprise 3%–5% of all testicular masses, with the most common being Leydig cell tumors (LCTs), and also include subtypes of Sertoli cell tumors (SCTs) and granulosa cell tumors.

LCTs. LCTs of the testis are rare sex cord stromal tumors that arise from the hormone secreting Leydig cells within the testis. Overall, they make up 1% of testicular tumors but are the single most common sex cord stromal tumor, accounting for 75% of the diagnoses in this group.[11] Masses may be bilateral in 3% of cases. While LCTs can exist at any age, classically a bimodal age distribution has been described with different presenting signs. In about 20% of cases, prepubertal males present with isosexual pseudoprecocity due to excessive androgen production. This is characterized by deepening of the voice, appearance of body hair, penile enlargement and advanced bone age.[12] They often do not have a palpable mass on examination, and US may even be insufficient to locate the source of excessive androgen production. Ultimately, differential testicular vein sampling may be required for a lateralizing diagnosis. This contrasts to adult patients, with an incidence peaking between 30 and 35 years old, who often present with a painless testicular mass and gynecomastia in 15%–30% of cases. LCTs have been associated with Klinefelter's syndrome, hereditary leiomyomatosis and renal cell carcinoma.[13,14] **While the vast majority of LCTs are benign, clinically malignant tumors may develop metastases in 10% of cases.** Other than the presence of metastasis, there appears to be no single histomorphological indicator for malignant LCTs.[15] It has been suggested that the presence of the following criteria may be indicative of LCTs that tend to metastasize: infiltrative borders, tumor size >5 cm, moderate or severe nuclear atypia, necrosis, lymphovascular invasion and >5 mitosis per 10 high-power fields (fig. 3).[16,17]

For the 90% of LCTs that are clinically localized to the testis, orchiectomy is often curative. Partial orchiectomy of peripheral masses <2.5 cm has been suggested as a safe option.[18] Overall, the cancer-specific mortality is <2%, with a 5-year survival of >90%.[19] In fact, Laclergerie et al demonstrated that TSS, when the diagnosis is confirmed by frozen section, does not compromise oncologic outcomes in regard to relapse-free survival if no risk factors are present.[20] Metastatic LCTs most commonly involve the retroperitoneal (RP) lymph nodes but can also spread to the lung, liver, bone and kidney.[21] Most reports describe the presence of metastases within the first 2 years of diagnosis; however, prolonged followup may be warranted as some patients have presented with metastatic disease 17 years after diagnosis.[22,23] **These tumors typically are chemoresistant, and surgical extirpation is the preferred approach. Overall, the prognosis for patients with metastatic LCT appears to be quite poor. As such, Calaway et al recently suggested that prophylactic primary retroperitoneal lymph node dissection (RPLND) should be considered in the setting of 1 or more pathological predictors of malignancy.[16]** The degree of increased risk based on predictors of malignancy is difficult to determine due to the rarity of the disease. However, most series show metastatic LCTs have at least 3 pathological risk factors.[16,17] In a recent meta-analysis including 1,375 patients with LCT, Fankhauser et al were able to design risk tables for metastatic disease with model AUCs of 0.93.[24] The authors consolidated the pathological risk predictors into 1 variable (yes/no) since clinicopathological risk factors were not reported in all studies. The presence of a protective pathological variable was also identified (presence of Reinke crystals, lipofuscin or gynecomastia). Age 42 years and tumor diameter 3 cm were identified as ideal cut points for localized and metastatic disease. The authors estimate >90% risk of metastatic disease in patients age ≥42 years, tumor size ≥3 cm, presence of at least 1 risk factor and absence of a protective factor, compared to less than 5% when the inverse values are present.

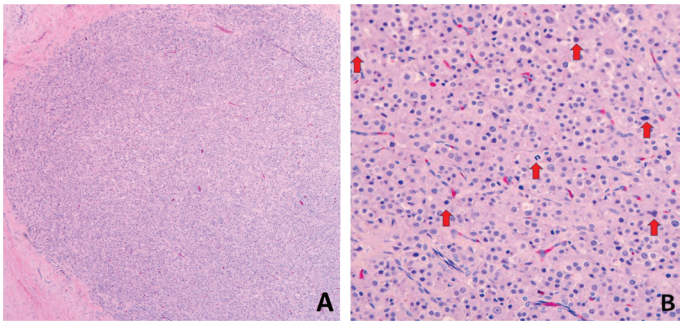

Figure 3. Photomicrographs of malignant LCT with known locally advanced disease. *A*, in low power, some areas of neoplasm form nodular aggregates that are separated by fibrous septa, which is common growth pattern in benign Leydig tumors. H&E, reduced from ×20. *B*, high-power view highlights moderate pleomorphism with strikingly increased mitotic figures (arrows). H&E, reduced from ×200. Reprinted with permission from Kern SQ, Speir RS, Akgul M et al: Rare benign and malignant testicular lesions: histopathology and management. Curr Opin Urol 2020; 30: 235.

SCTs. SCTs of the testis are the second most common sex cord stromal tumor, although they are still quite rare, representing only 0.4%–1.5% of testicular masses.[25] While they can occur at any age, with 15% presenting in children, they typically present in the third or fourth decade of life (mean age 39 years).[26] As with other sex cord stromal tumors, SCTs classically present as a painless testicular mass. These cases may also present with erectile dysfunction or gynecomastia due to exogenous estradiol production. On US, they generally appear as well-defined hypoechoic lesions without any distinguishing features from other benign or malignant testicular lesions. Initial management of these lesions is orchiectomy or TSS for small peripherally located lesions when intraoperative frozen section confirms SCT. Approximately a third of patients have an associated genetic syndrome or endocrine abnormality,[27] the most common being the autosomal dominant Peutz-Jeghers syndrome, characterized by mucocutaneous pigmentation and hamartomatous intestinal polyposis,

and Carney syndrome, leading to myxomas of the skin, soft tissue and heart. Cushing's disease, pituitary adenomas and schwannoma can also occur.

Clinically, malignant SCT is rare, occurring in only 15% of cases. Malignancy can only be accurately diagnosed in the presence of metastases. **Due to this and the chemoresistant and radioresistant nature of this tumor, the prognosis is quite poor.[28]** These tumors, as with a majority of other malignant testis tumors, classically metastasize to the RP lymph nodes. Primary RPLND has been suggested when RP disease is present, although Calaway et al demonstrated poor recurrence-free survival (RFS) and overall survival (OS) in all patients in their series who developed RP disease recurring after a mean of 9.7 months and dying of disease 29.8 months after surgery.[16] **As such, it was their recommendation to consider primary RPLND for all patients with clinical stage I disease before disease spread to the retroperitoneum when they have 1 or more adverse pathological features on orchiectomy (infiltrative borders, tumor size >5 cm, moderate or severe nuclear atypia, necrosis, lymphovascular invasion and >5 mitoses per 10 high-power fields).** Similar to LCT, early consideration of RPLND for resection of potential micrometastatic disease can be exercised due to the poor prognosis of sex cord stromal tumors.[16,24]

Granulosa cell tumors. Granulosa cell tumors have 2 subtypes: juvenile and adult-type. **This tumor is the most common testicular mass among males less than 6 months of age.[29]** The juvenile type is considered to be a benign entity as there have been no reported cases of metastatic disease in this age group. In the postpubertal male, the majority present with a painless mass.[30] The mass may produce estradiol, which can account for the bilateral painless gynecomastia in 17% of men.[31] There are no ultrasonographic characteristics that have been shown to clearly distinguish granulosa cell tumors from other testicular masses, both benign and malignant.[32]

Adult granulosa cell tumors may exhibit malignant features in 25% of cases. Even after orchiectomy, the only histopathological criteria shown to be associated with malignancy was size >5.0 cm; patient age, mitotic activity, tumor necrosis and the presence of gynecomastia did not predict malignant behavior.[33] In regard to both treatment and surveillance recommendations, the literature is inconclusive based on low numbers of reported cases. While slow growing, they have the potential to metastasize many years after the initial diagnosis. A review of previous studies estimated the metastatic frequency is 16%.[34] Sites of metastasis include the RP lymph nodes, liver, bone and lungs. Patients presenting with distant metastatic disease outside the retroperitoneum have a very poor prognosis. Hammerich et al found that all 3 patients presenting with disease outside the retroperitoneum progressed quickly and died of disease. This is in contrast to patients presenting with metastases to the retroperitoneum only, which may allow for surgical treatment, thus leading to a more durable response.[35] **Men who undergo orchiectomy demonstrating granulosa cell tumors should undergo extended followup due to the delayed metastatic potential.[32]**

MISCELLANEOUS BENIGN TUMORS

Lipomas are the most common benign paratesticular tumor across all ages (45%).[27] They are usually located along the spermatic cord. US reveals a homogeneous hyperechoic lesion, and computerized tomography (CT) and magnetic resonance imaging (MRI) may be used to help exclude liposarcoma in large lesions. Features that suggest liposarcoma include increased patient age; lesion size >10 cm; presence of thick septa; presence of nodular, globular or non-adipose mass-like areas; and decreased fat composition (less than 75% fat).[36] Gaskin and Helms prospectively reviewed 126 grossly fatty masses and showed MRI was 100% specific for lipoma whenever a grossly fatty mass had few or no thin septa or no enhancement, and minimal or no areas of high T2 signal.[37] Local excision of a lipoma is reserved for symptomatic relief.

Testicular hemangiomas are rare, can occur at all ages and have no associated factors predisposing to their development.[27,38] While infantile hemangiomas are common, testicular hemangiomas comprise less than 1% of cases, typically have a rapid postnatal growth and spontaneously regress during childhood.[27,39] They are usually asymptomatic but can cause pain, bleeding or ulceration. Ulceration of infantile hemangiomas occurs in 5%–13% of cases, and while testicular hemangiomas are normally deep tumors with a far lower risk of ulceration, this is a potential complication to consider with increased size or close involvement of the scrotal skin. Testicular hemangiomas can appear as a varicocele; however, most lesions exhibit sonographic features similar to malignant tumors, appearing as focal hypoechoic lesions with increased vascularity.[40] Surgical excision is diagnostic and therapeutic.

Testicular adrenal rest tumors can be seen in adrenogenital syndrome. They tend to appear as bilateral masses in patients with underlying congenital adrenal hyperplasia (CAH).[41] They often present before age 9 years due to symptoms related to CAH (vomiting, diarrhea, dehydration, enlargement of the genitalia or sexual precocity); however, patients may present at later ages should CAH be in the mild salt-preserving form.[42] **In the adult population, adrenogenital syndrome should be suspected in males presenting with infertility and bilateral testicular masses.[43]** These benign masses are a diagnostic dilemma both clinically and pathologically, and are often identified after orchiectomy, particularly if CAH is unrecognized. The diagnosis can be facilitated by laboratory evaluation finding elevated adrenocorticotropic hormone, urinary 17KS, 17-hydroxyprogesterone, elevated serum testosterone, dehydroepiandrosterone (DHEA) and androstenedione.[42] Pathologically, they are frequently mistaken for LCTs due to the overlapping histological characteristics.[41,44] Testicular adrenal rest tumors regress in up to 75% of cases with steroid replacement therapy, obviating the need for surgical therapy.[42] In patients with non-hormone responsive tumors, orchiectomy was traditionally performed, although reports of TSS or observation have demonstrated a safe alternative to this paradigm.[41,45] A TSS approach is an important consideration, especially in cases of bilateral masses, since males with CAH are potentially fertile.

RARE MALIGNANT TUMORS

While non-germ cell tumors are more commonly attributed to metastatic disease to the testicle, it is important to be familiar with rare primary non-germ cell tumors seen in practice. All suspicious testicular masses should be evaluated by physical examination, imaging and STMs. Surgical management through the inguinal approach should be considered in all patients with concerning testicular masses on examination or radiographic studies. High ligation of the spermatic cord to the level of the internal inguinal ring should be maintained. **A TSS via inguinal**

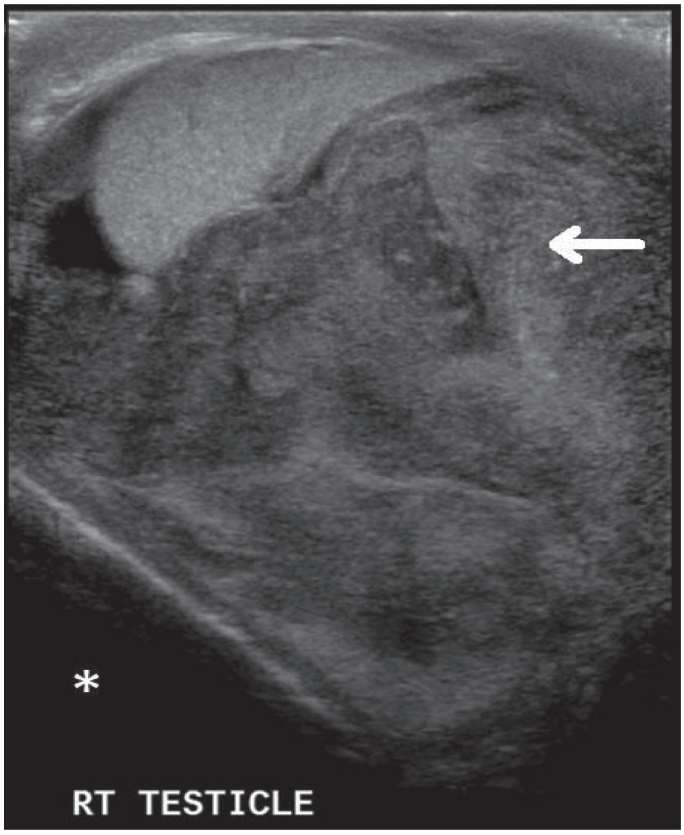

Figure 4. Ultrasound images of heterogeneous testicle replaced by mass (arrow) associated with large hydrocele (asterisk). Vascular flow was present. Pathology revealed testicular RMS. *RT*, right.

approach with temporary occlusion of the spermatic cord can be considered in highly selected patients with small testicular masses (<2 cm) with equivocal US/physical examination findings; negative STMs; congenital, acquired or functionally solitary testis; or bilateral synchronous tumors after thorough counseling of the risks and benefits during the shared decision-making process with the patient.[46]

Sarcomas. There are many rare types of primary sarcoma seen in the paratestis and testis arising from mesenchymal, epithelial and mesothelial cells, most commonly from the epididymis, spermatic cord and tunica vaginalis; however, intratesticular sarcomas have been described.[47,48] These sarcomas include liposarcoma, embryonal or alveolar rhabdomyosarcoma (RMS), leiomyosarcoma, myosarcoma, chondrosarcoma and osteosarcoma.[48,49] They most commonly present as an enlarging painless testicular mass. **US is non-specific and typically shows disorganized, possibly infiltrative, solid masses with heterogeneity and hypervascularity, which can be associated with a hydrocele or thickening of the tunica vaginalis (fig. 4).**[50] Obtaining an MRI may be useful in differentiating the structures involved for staging, and even gadolinium-enhanced imaging can aid in differentiating a benign cystic lesion and a cystic neoplasm.[51–53] **It is critical to rule out metastatic spread to the testicle, and orchiectomy is occasionally performed to obtain tissue diagnosis depending on the location of the primary sarcoma.** Histological analysis reveals a highly vascular tumor with stromal elements consistent with the sarcoma type. For instance, testicular liposarcoma will have atypical hyperchromatic nuclei with fibrosis and adipose tissue (fig. 5).

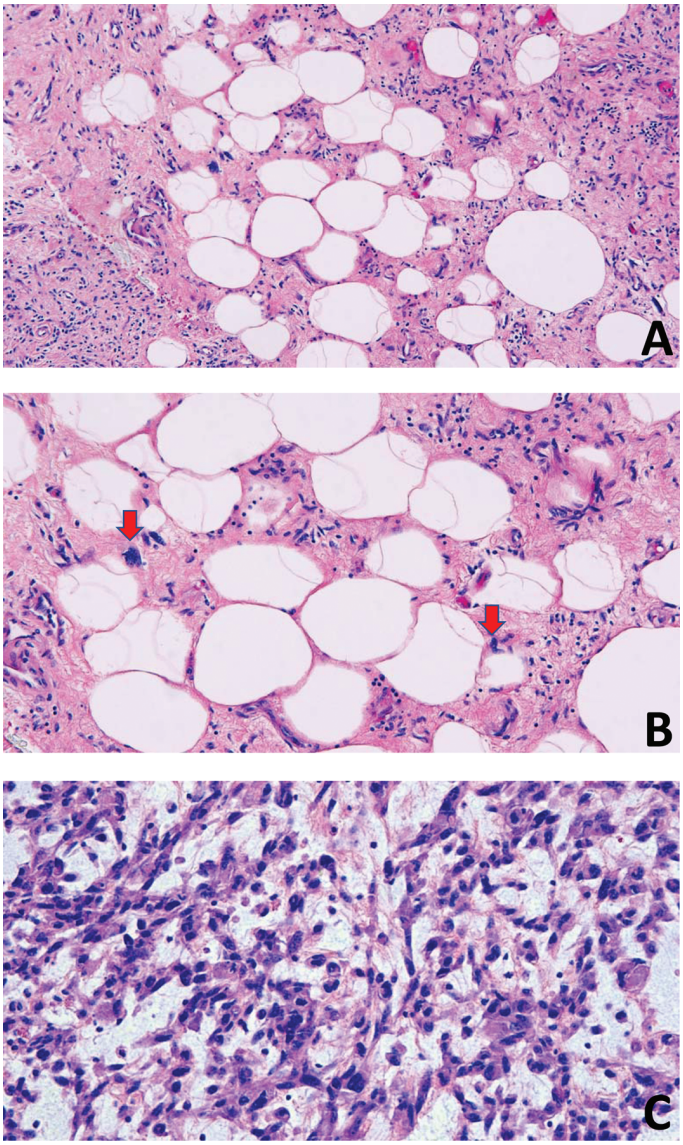

Figure 5. *A*, well-differentiated liposarcoma is most common sarcoma of paratestis. H&E, reduced from ×40. *B*, delicate fibrosis is intermingled with adipose tissue with frequent atypical hyperchromatic nuclei (arrows) inside fibrous tissue (or adipose tissue, not shown). H&E, reduced from ×100. *C*, occasionally, dedifferentiation occurs in this entity, mostly in undifferentiated pleomorphic lipoma morphology, with large bizarre cells with marked anisocytosis and increased mitosis. H&E, reduced from ×200. Reprinted with permission from Kern SQ, Speir RS, Akgul M et al: Rare benign and malignant testicular lesions: histopathology and management. Curr Opin Urol 2020; **30:** 235.

Due to the rarity of paratesticular or testicular sarcomas, established management and long-term followup are still unclear. Inguinal orchiectomy with high ligation of the spermatic cord, with care to ensure negative margins, is recommended for primary sarcomas. **In patients with a positive margin after the initial resection, aggressive wide re-resection of positive margin, and even hemiscrotectomy in certain cases, has improved disease-free survival and OS.**[49,53,54] The importance of obtaining negative margins cannot be overemphasized. Khandekar et al showed in 25 cases of paratesticular liposarcoma that local

RFS is negatively impacted by positive margins, with 29% vs 100% RFS at 3 years, despite radiation therapy (RT) in those with positive margins.[55] **Adjuvant radiation has shown efficacy in decreasing rates of local recurrence in extremity sarcomas; however, this does not translate into definitive local control for non-extremity soft tissue sarcomas.[56]** With regard to paratesticular sarcomas, the rarity of the disease makes it hard to determine if radiation has a therapeutic benefit. Coleman et al reported no therapeutic benefit with adjuvant radiation in their retrospective review of 21 patients.[49] Conversely, Catton et al[57] had 100% local control of disease in 6 patients, and Cerda et al[58] observed no recurrence in all 5 patients at 18-month median followup. However, conclusions are difficult to draw due to the small number of patients in these studies. Likewise, chemotherapy has not proven beneficial.[47,53,54,59] The surgical management of sarcoma varies based on the type of sarcoma. **RPLND usually is not beneficial unless there are suspiciously enlarged nodes on imaging or in cases of RMS, which have a significant propensity to spread to the retroperitoneum in 40%–60% of patients.** Conversely, the more common subtypes, liposarcomas and leiomyosarcomas, spread and recur by direct invasion.[53,60,61]

As previously discussed, the management of RMS slightly differs from that of other sarcoma subtypes due to the higher propensity for metastasis to the retroperitoneum. The majority of literature stems from the pediatric population where paratesticular RMS accounts for 12% of all pediatric scrotal tumors.[27] Poor prognostic indicators include alveolar histology, age older than 7 years, unresectable RP disease, and distant metastatic spread.[27] Historically, a RPLND in these patients at the time of diagnosis was controversial. Certain centers considered a RP dissection therapeutic in addition to contributing to improved staging, while some argued that chemotherapy alone is able to eradicate micrometastases.[62,63] Investigators at Indiana University reviewed their experience with 19 patients over 14 years of age from 1980 to 1997 with negative lymphadenopathy on imaging or RP only disease, finding a thorough RP resection in conjunction with multiagent chemotherapy was effective with 17 patients (89%) disease-free at a mean of 6.4 years while 2 patients died of disease that recurred outside of the retroperitoneum.[64] One quarter to three-quarters of patients have lymph node metastases at presentation, leading the IRSG (Intergroup Rhabdomyosarcoma Study Group) to establish guidance for treating these rare tumors. **RPLND and multiagent chemotherapy with vincristine, actinomycin D and cyclophosphamide after radical inguinal orchiectomy is now recommended in males greater than 10 years old, regardless of stage, and boys younger than 10 years with evidence of RP disease.[27]** The risk-based IRSG treatment protocols are comprehensive; however, a thorough RPLND with an R0 resection is a favorable prognostic factor that may save the patient RT and the addition of topotecan or irinotecan to the chemotherapy protocol.[65]

Adenocarcinoma of the rete testis. Adenocarcinoma of the rete testis is a rare tumor with fewer than 100 cases reported and tends to occur in men over the age of 60 years.[66,67] Most patients present with a mass or testicular swelling (66%), hydrocele (36%) and pain (22%).[68] **It is a locally aggressive neoplasm, with more than half of cases metastatic at diagnosis.[69] It has a poor prognosis, with 3- and 5-year disease-free survival of 45%–49% and 13%–20%, respectively.[67,68]**

Nochomovitz and Orenstein refined the diagnostic criteria to include: absence of histologically similar extrascrotal tumor that could be the primary site, tumor centered in the hilum of the testis, morphology incompatible with any other type of testicular or paratesticular tumor, and immunohistochemical exclusion of other possibilities.[66] Appropriate evaluation includes tumor markers (which will yield negative results), scrotal US and staging imaging evaluating for metastatic disease. The clinical applicability of positron emission tomography (PET)-CT is debatable as some have reported improved detection of RP disease metastasis over conventional CT, while others have reported metastatic disease found in the landing zone at RPLND in the setting of normal PET-CT imaging.[67,70]

The rarity of the disease makes the establishment of definitive management recommendations difficult; however, several reports suggest poor response rates to systemic chemotherapy and RT.[67,68,71,72] The hilar location, with its proximity to lymphatic drainage, and the low to intermediate proliferative index, as reflected by mitotic rate and Ki-67, are potential reasons for metastasis and resistance to chemotherapy or RT.[68] **Although radical orchiectomy alone in patients may have some benefit, a full bilateral RPLND for localized disease and surgical removal of resectable distant disease are recommended.[69,72]** One study found that of patients who underwent full template RPLND 5/5 were disease-free at a mean of 33 months (1 patient was found to have low volume disease in a single lymph node) compared to only 2 of 6 patients treated with orchiectomy alone for local disease.[72] While orchiectomy may be curative, there is no way to predict which patients will respond to orchiectomy alone, thus highlighting the importance of RPLND before clinical stage II metastasis develops. Sanchez-Chapado et al performed a meta-analysis of 40 cases and found higher 3-year OS in those who underwent RPLND vs those who did not have RP surgery (83% vs 42%, log rank p=0.03).[69] The group also found that organ-confined disease smaller than 5 cm was an independent predictor of survivability but was not associated with tumor stage or histological growth pattern (nodular infiltrating vs predominantly cystic).[69]

Mesothelioma. Mesothelioma of the testicle and paratesticular structures is a rare neoplasm of mesenchymal origin. It represents less than 5% of mesotheliomas, which have more common origins from the mesothelial lining of pleural or peritoneal cavities.[73] Patients most commonly present between the sixth and eighth decade of life with a painless intrascrotal mass, with a hydrocele present in over half of cases.[74,75] Evaluation includes US imaging for metastatic disease and tumor markers. **This malignancy is often found intraoperatively or postoperatively after hydrocelectomy, inguinal herniorrhaphy or scrotal exploration as it usually mimics common inguinal or scrotal disease and goes unrecognized.[75,76]** In our experience, we have not noted reproducible US findings pathognomonic for mesothelioma. Several prognostic factors have been identified, including age >60 years at diagnosis, presence of metastatic disease at diagnosis and asbestos exposure.[75,77,78]

A recent review including 113 patients from 1973 to 2015 identified that 5-year OS vs disease-specific survival for all patients was 49% vs 58%, and 10-year OS vs disease-specific survival was 33% vs 45%.[74] Furthermore, biphasic mesotheliomas were associated with worse OS compared to general mesotheliomas and epithelioid subtypes, in addition to the finding that tumors greater than 4 cm were associated with significantly worse oncologic outcomes. Aggressive surgical excision along with combination pemetrexed and cisplatin chemotherapy is the predominant therapy of choice.[75,79] While there are limited data

on RT for testicular and paratesticular mesothelioma, there is no evidence of prolonged survival in pleural mesothelioma, and thus this approach is largely reserved for palliation.[74,80]

Primary testicular lymphoma. **Primary testicular non-Hodgkin lymphoma accounts for approximately 9% of testicular neoplasms and is the most common testicular malignancy in the elderly.[81]** Patients most commonly present clinically with unilateral painless scrotal swelling, sometimes with sharp scrotal pain or hydrocele. Bilateral testicular involvement is detected in up to 35% cases at the time of diagnosis.[82] Testicular lymphoma commonly disseminates to other extranodal organs, such as the contralateral testis, central nervous system (CNS), lung, pleura and Waldeyer's ring soft tissue.[81,82] Since primary testicular lymphoma develops in an immune-privileged site behind the blood-testis barrier, there is a higher risk of CNS or contralateral testicular relapse.[83] **Outside of radical orchiectomy, the role of surgery is limited to palliation of symptoms or to relieve upper tract obstruction in patients with large volume RP disease.**

For patients with limited disease, the recommended first-line treatment is rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone (R-CHOP), with CNS prophylaxis consisting of intrathecal methotrexate and prophylactic irradiation of the contralateral testis (30 Gy), and stage II patients also receiving RT (30–36 Gy) to regional lymph nodes.[83–86] With this regimen, Vitolo et al published the largest prospective multicenter trial showing 52 patients (98%) achieved a complete response, and with a median followup of 65 months the 5-year progression-free survival was 74% and OS was 85%.[86] The regimen decreased the cumulative incidence of CNS relapse at 5 years to 6% from the previously observed 5- and 10-year rates of 20% and 35%, respectively.[86,87] The absence of contralateral testis relapses in this trial confirmed the efficacy of prophylactic RT to the contralateral testis. In a previous multicenter retrospective trial by the International Extranodal Lymphoma Study Group involving 373 patients, prophylactic RT reduced contralateral testis relapse to 8%, compared to 35% in those not irradiated.[87] Should relapse occur, a contralateral orchiectomy is recommended. For patients initially diagnosed with bilateral testicular lymphomas, a bilateral orchiectomy is performed followed by R-CHOP and CNS prophylaxis.

CONCLUSION

Diagnosis and management of rare benign and malignant testicular tumors vary widely. However, the initial evaluation and diagnosis should be consistent with those of germ cell tumors with regard to examination, laboratory analysis and imaging. **Regardless of pathology, continued patient self-testicular examinations should be emphasized.** Management should adhere to oncologic principles. Vascular intratesticular masses should be considered malignant until proven otherwise by pathological analysis. Malignant non-germ cell tumors display biologically aggressive characteristics, which often drive poor recurrence and survivability outcomes. As our knowledge of these diseases increases, hopefully this will lead to improvements in management and prognosis.

DID YOU KNOW?

- All suspicious testicular masses should be evaluated by physical examination, imaging and serum tumor markers.
- Sex cord stromal tumors are typically chemoresistant, and surgical extirpation is the preferred approach.
- Due to the rarity of sarcomas and the difference in management between subtypes, patients should be treated by an experienced multidisciplinary team of sarcoma specialists.
- Imaging characteristics of benign and malignant non-germ cell tumors are often indistinguishable and can have a similar appearance to testicular germ cell tumors.
- Surgical management through an inguinal approach should be considered in all patients with concerning testicular masses on examination or radiographic studies.

Table. Assessment of all tumors involved examination, STMs and radiographic imaging

Tumor	Presenting Symptoms	Radiographic Findings	Treatment	Pathological Characteristics	Metastatic Potential
Epidermoid and dermoid cysts	Painless testicular mass	"Onion ring" laminated appearance on US	Radical or partial orchiectomy	Surrounding germ cell neoplasia in situ indicates malignant postpubertal-type teratoma	Benign
Adrenogenital syndrome tumors	Infertility, bilateral masses, CAH	Heterogeneous hypoechoic intratesticular mass	Steroid replacement, surgery if refractory	Often have elevated adrenocorticotropic hormone, DHEA, testosterone, 17-hydroxyprogesterone, androstenedione	Benign
Hemangiomas	Usually asymptomatic	Can mimic malignant tumors	Surgical excision	Risk of ulceration with large tumors or if close to scrotal skin	Benign
Adenomatoid tumors	Slow growing painless paratesticular mass	Vascular paratesticular or intratesticular mass	Radical or partial orchiectomy	30% of paratesticular masses	Benign
Sex cord tumors					
Leydig cell	Can have excess androgen production	US may not show testicular mass, testicular vein sampling may be needed to lateralize tumors	Radical orchiectomy, primary RPLND if >1 risk factor present	Risk factors: >5 cm, necrosis, moderate/severe nuclear atypia, lymphovascular invasion, infiltrating margins, >5 mitotic figures per 10 high-power fields	10% malignant
Sertoli cell	Can have excess androgen production	Well-defined vascular mass on US, no discernible features from benign or malignant tumors	Radical orchiectomy, primary RPLND if >1 risk factor present	Risk factors: >5 cm, necrosis, moderate/severe nuclear atypia, lymphovascular invasion, infiltrating margins, >5 mitotic figures per 10 high-power fields	15% malignant
Granulosa cell	Most common in males <6 mos old	Well-defined vascular mass on US, no discernible features from benign or malignant tumors	Radical or partial orchiectomy	Adults need extended surveillance due to metastatic potential	Children—benign, adults—25% malignant
Sarcomas	Testicular or paratesticular mass	Often associated with hydrocele or thickening of tunica vaginalis. MRI may be useful for staging	Radical orchiectomy. RPLND not beneficial unless RP disease or RMS is present	Highly vascular tumor with stromal elements consistent with sarcoma type. RMS has high propensity for metastasis	Malignant
Adenocarcinoma of the rete testis	Testicular mass/swelling, hydrocele, pain	50% metastatic at diagnosis	Radical orchiectomy, RPLND	Immunohistochemistry is often needed for diagnosis and differentiation from mesothelioma	Malignant
Mesothelioma	Often mimics benign pathology	No distinguishable US features	Aggressive surgical resection with combination chemotherapy	Associated with asbestos exposure	Malignant
Primary testicular lymphoma	Most common elderly testis malignancy	Vascular homogeneous intratesticular mass on US	R-CHOP chemotherapy, RT to contralateral testis, consider CNS prophylaxis	Disseminates to contralateral testis, CNS, lung, pleura, and Waldeyer's ring	Malignant

REFERENCES

1. Shah KH, Maxted WC and Chun B: Epidermoid cysts of the testis: a report of three cases and an analysis of 141 cases from the world literature. Cancer 1981; **47:** 577.
2. Pohl HG, Shukla AR, Metcalf PD et al: Prepubertal testis tumors: actual prevalence rate of histological types. J Urol 2004; **172:** 2370.
3. Ulbright TM and Srigley JR: Dermoid cyst of the testis: a study of five postpubertal cases, including a pilomatrixoma-like variant, with evidence supporting its separate classification from mature testicular teratoma. Am J Surg Pathol 2001; **25:** 788.
4. Cheng L, Zhang S, MacLennan GT et al: Interphase fluorescence in situ hybridization analysis of chromosome 12p abnormalities is useful for distinguishing epidermoid cysts of the testis from pure mature teratoma. Clin Cancer Res 2006; **12:** 5668.
5. Wang WP, Guo C, Berney DM et al: Primary carcinoid tumors of the testis: a clinicopathologic study of 29 cases. Am J Surg Pathol 2010; **34:** 519.
6. Walsh C and Rushton HG: Diagnosis and management of teratomas and epidermoid cysts. Urol Clin North Am 2000; **27:** 509.
7. Woo LL and Ross JH: The role of testis-sparing surgery in children and adolescents with testicular tumors. Urol Oncol 2016; **34:** 76.
8. Amin W and Parwani AV: Adenomatoid tumor of testis. Clin Med Pathol 2009; **2:** 17.
9. Paffenholz P, Held L, Loosen SH et al: Testis sparing surgery for benign testicular masses: diagnostics and therapeutic approaches. J Urol 2018; **200:** 353.
10. Goode B, Joseph NM, Stevers M et al: Adenomatoid tumors of the male and female genital tract are defined by TRAF7 mutations that drive aberrant NF-kB pathway activation. Mod Pathol 2018; **31:** 660.
11. Eble JN, Sauter G, Epstein J et al: World Health Organization Classification of Tumours: Pathology and Genetics of Tumours of the Urinary System and Male Genital Organs, 3rd ed. Lyon, France: International Agency for Research on Cancer Press 2004; pp 252–255.
12. Mukhopadhyay M, Das C, Sarkar S et al: Leydig cell tumor of testis in a child: an uncommon presentation. J Indian Assoc Pediatr Surg 2017; **22:** 181.
13. Soria JC, Durdux C, Chretien Y et al: Malignant Leydig cell tumor of the testis associated with Klinefelter's syndrome. Anticancer Res 1999; **19:** 4491.
14. Carvajal-Carmona LG, Alam NA, Pollard PJ et al: Adult Leydig cell tumors of the testis caused by germline fumarate hydratase mutations. J Clin Endocrinol Metab 2006; **91:** 3071.
15. Mooney KL and Kao CS: A contemporary review of common adult non-germ cell tumors of the testis and paratestis. Surg Pathol Clin 2018; **11:** 739.
16. Calaway AC, Tachibana I, Masterson TA et al: Oncologic outcomes following surgical management of clinical stage II sex cord stromal tumors. Urology 2019; **127:** 74.
17. Kim I, Young RH and Scully RE: Leydig cell tumors of the testis. A clinicopathological analysis of 40 cases and review of the literature. Am J Surg Pathol 1985; **9:** 177.
18. Suardi N, Strada E, Colombo R et al: Leydig cell tumour of the testis: presentation, therapy, long-term follow-up and the role of organ-sparing surgery in a single-institution experience. BJU Int 2009; **103:** 197.
19. Banerji JS, Odem-Davis K, Wolff EM et al: Patterns of care and survival outcomes for malignant sex cord stromal testicular cancer: results from the National Cancer Data Base. J Urol 2016; **196:** 1117.
20. Laclergerie F, Mouillet G, Frontczak A et al: Testicle-sparing surgery versus radical orchiectomy in the management of Leydig cell tumors: results from a multicenter study. World J Urol 2018; **36:** 427.
21. Grem JL, Robins HI, Wilson KS et al: Metastatic Leydig cell tumor of the testis. Report of three cases and review of the literature. Cancer 1986; **58:** 2116.
22. Bertram KA, Bratloff B, Hodges GF et al: Treatment of malignant Leydig cell tumor. Cancer 1991; **68:** 2324.
23. Gulbahce HE, Lindeland AT, Engel W et al: Metastatic Leydig cell tumor with sarcomatoid differentiation. Arch Pathol Lab Med 1999; **123:** 1104.
24. Fankhauser CD, Grogg JB, Hayoz S et al: Risk factors and treatment outcomes of 1,375 patients with testicular Leydig cell tumors: analysis of published case series data. J Urol 2020; **203:** 949.
25. Ohr J: Tumors of the testis, adnexa, spermatic cord, and scrotum. Arch Pathol Lab Med 2000; **124:** 1855.
26. Osbun N, Winters B, Holt SK et al: Characteristics of patients with Sertoli and Leydig cell testis neoplasms from a national population-based registry. Clin Genitourin Cancer 2017; **15:** e263.
27. Ahmed HU, Arya M, Muneer A et al: Testicular and paratesticular tumours in the prepubertal population. Lancet Oncol 2010; **11:** 476.
28. Mosharafa AA, Foster RS, Bihrle R et al: Does retroperitoneal lymph node dissection have a curative role for patients with sex cord-stromal testicular tumors? Cancer 2003; **98:** 753.
29. Shukla AR, Huff DS, Canning DA et al: Juvenile granulosa cell tumor of the testis: contemporary clinical management and pathological diagnosis. J Urol 2004; **171:** 1900.
30. Abdallat M and Al-Samen AA: Granulosa cell tumor of the adult testis. J Res Med Sci 2001; **18:** 64.
31. Bing Z and Bai S: Gynecomastia: an uncommon but important clinical manifestation for testicular tumors. OJPathology 2012; **2:** 6.
32. Tsitouridis I, Maskalidis C, Sdrolia A et al: Adult type granulosa cell tumor of the testis: radiological evaluation and review of the literature. Turk J Urol 2014; **40:** 115.
33. Hanson JA and Ambaye AB: Adult testicular granulosa cell tumor: a review of the literature for clinicopathologic predictors of malignancy. Arch Pathol Lab Med 2011; **135:** 143.
34. Cornejo KM and Young RH: Adult granulosa cell tumors of the testis: a report of 32 cases. Am J Surg Pathol 2014; **38:** 1242.
35. Hammerich KH, Hille S, Ayala GE et al: Malignant advanced granulosa cell tumor of the adult testis: case report and review of the literature. Hum Pathol 2008; **39:** 701.
36. Kransdorf MJ, Bancroft LW, Peterson JJ et al: Imaging of fatty tumors: distinction of lipoma and well-differentiated liposarcoma. Radiology 2002; **224:** 99.
37. Gaskin CM and Helms CA: Lipomas, lipoma variants, and well-differentiated liposarcomas (atypical lipomas): results

of MRI evaluations of 126 consecutive fatty masses. AJR Am J Roentgenol 2004; **182:** 733.
38. Kryvenko ON and Epstein JI: Testicular hemangioma: a series of 8 cases. Am J Surg Pathol 2013; **37:** 860.
39. Fernandez-Pineda I and Parida L: Testicular haemangiomas and vascular malformations. Lancet Oncol 2010; **11:** 814.
40. Ben Abda R, Bess D and Nieves-Robbins N: Testicular hemangioma mimicking a malignant neoplasm. Radiol Case Rep 2016; **11:** 121.
41. Rich MA, Keating MA, Levin HS et al: Tumors of the adrenogenital syndrome: an aggressive conservative approach. J Urol 1998; **160:** 1838.
42. Rutgers JL, Young RH and Scully RE: The testicular "tumor" of the adrenogenital syndrome. A report of six cases and review of the literature on testicular masses in patients with adrenocortical disorders. Am J Surg Pathol 1988; **12:** 503.
43. Claahsen-van der Grinten HL, Hermus ARMM and Otten BJ: Testicular adrenal rest tumours in congenital adrenal hyperplasia. Int J Pediatr Endocrinol 2009; **2009:** 624823.
44. Martinez-Aguayo A, Rocha A, Rojas N et al: Testicular adrenal rest tumors and Leydig and Sertoli cell function in boys with classical congenital adrenal hyperplasia. J Clin Endocrinol Metab 2007; **92:** 4583.
45. Walker BR, Skoog SJ, Winslow BH et al: Testis sparing surgery for steroid unresponsive testicular tumors of the adrenogenital syndrome. J Urol 1997; **157:** 1460.
46. Stephenson A, Eggener SE, Bass EB et al: Diagnosis and treatment of early stage testicular cancer: AUA guideline. J Urol 2019; **202:** 272.
47. Keenan RA, Nic An Riogh AU, Stroiescu A et al: Paratesticular sarcomas: a case series and literature review. Ther Adv Urol 2019; **11:** 1756287218818029.
48. Ulbright TM and Young RH: Testicular and paratesticular tumors and tumor-like lesions in the first 2 decades. Semin Diagn Pathol 2014; **31:** 323.
49. Coleman J, Brennan MF, Alektiar K et al: Adult spermatic cord sarcomas: management and results. Ann Surg Oncol 2003; **10:** 669.
50. Rypens F, Garel L, Franc-Guimond J et al: Paratesticular rhabdomyosarcoma presenting as thickening of the tunica vaginalis. Pediatr Radiol 2009; **39:** 1010.
51. Akbar SA, Sayyed TA, Jafri SZ et al: Multimodality imaging of paratesticular neoplasms and their rare mimics. Radiographics 2003; **23:** 1461.
52. Kim W, Rosen MA, Langer JE et al: US MR imaging correlation in pathologic conditions of the scrotum. Radiographics 2007; **27:** 1239.
53. Goldberg H, Wong L-M, Dickson B et al: Long-term oncological outcomes of patients with paratesticular sarcoma. BJU Int 2019; **124:** 801.
54. Murray KS, Vertosick EA, Spaliviero M et al: Importance of wide re-resection in adult spermatic cord sarcomas: report on oncologic outcomes at a single institution. J Surg Oncol 2018; **117:** 1464.
55. Khandekar MJ, Raut CP, Hornick JL et al: Paratesticular liposarcoma: unusual patterns of recurrence and importance of margins. Ann Surg Oncol 2013; **20:** 2148.
56. Strander H, Turesson I and Cavallin-Stahl E: A systematic overview of radiation therapy effects in soft tissue sarcomas. Acta Oncol 2003; **42:** 516.
57. Catton C, Jewett M, O'Sullivan B et al: Paratesticular sarcoma: failure patterns after definitive local therapy. J Urol 1999; **161:** 1844.
58. Cerda T, Martin E, Truc G et al: Safety and efficacy of intensity-modulated radiotherapy in the management of spermatic cord sarcoma. Cancer Radiother 2017; **21:** 16.
59. Sarcoma Meta-Analysis Collaboration: Adjuvant chemotherapy for localised resectable soft-tissue sarcoma of adults: meta-analysis of individual data. Lancet 1997; **350:** 1647.
60. Rodriguez D and Olumi AF: Management of spermatic cord tumors: a rare urologic malignancy. Ther Adv Urol 2012; **4:** 325.
61. Moroni M, Nesi G, Travaglini F et al: Rhabdomyosarcoma of the spermatic cord. A case report with review of the literature. Urol Int 2003; **71:** 114.
62. Olive D, Flamant F, Zucker JM et al: Paraaortic Lymphadenectomy is not necessary in the treatment of localized paratesticular rhabdomyosarcoma. Cancer 1984; **54:** 1283.
63. Goldfarb B, Khoury AE, Greenberg ML et al: The role of retroperitoneal lymphadenectomy in localized paratesticular rhabdomyosarcoma. J Urol 1994; **152:** 785.
64. Hermans BP, Foster RS, Bihrle R et al: Is retroperitoneal lymph node dissection necessary for adult paratesticular rhabdomyosarcoma? J Urol 1998; **160:** 2074.
65. Raney RB, Anderson JR, Barr FG et al: Rhabdomyosarcoma and undifferentiated sarcoma in the first two decades of life: a selective review of Intergroup Rhabdomyosarcoma Study Group experience and rationale for Intergroup Rhabdomyosarcoma Study V. J Pediatr Hematol Oncol 2001; **23:** 215.
66. Nochomovitz LE and Orenstein JM: Adenocarcinoma of the rete testis. Case report, ultrastructural observations, and clinicopathologic correlates. Am J Surg Pathol 1984; **8:** 625.
67. Maganty A, Fombona A, Bandari J et al: Aggressive surgical management of adenocarcinoma of the rete testis. Urol Case Rep 2018; **16:** 72.
68. Al-Obaidy KI, Idrees MT, Grignon DJ et al: Adenocarcinoma of the rete testis: clinicopathologic and immunohistochemical characterization of 6 cases and review of the literature. Am J Surg Pathol 2019; **43:** 670.
69. Sanchez-Chapado M, Angulo JC and Haas GP: Adenocarcinoma of the rete testis. Urology 1995; **46:** 468.
70. Musser JE, Ernest AJ, Thibault GP et al: Primary adenocarcinoma of the rete testis: improved staging accuracy with CT-PET. Urology 2011; **77:** 334.
71. Burns MW, Chandler WL and Krieger JN: Adenocarcinoma of rete testis. Role of inguinal orchiectomy plus retroperitoneal lymph node dissection. Urology 1991; **37:** 571.
72. Stein JP, Freeman JA, Esrig D et al: Papillary adenocarcinoma of the rete testis: a case report and review of the literature. Urology 1994; **44:** 588.
73. Chekol SS and Sun CC: Malignant mesothelioma of the tunica vaginalis testis: diagnostic studies and differential diagnosis. Arch Pathol Lab Med 2012; **136:** 113.
74. Nazemi A, Nassiri N, Pearce S et al: Testicular mesothelioma: an analysis of epidemiology, patient outcomes, and prognostic factors. Urology 2019; **126:** 140.
75. Recabal P, Rosenzweig B, Bazzi WM et al: Malignant mesothelioma of the tunica vaginalis testis: outcomes following

surgical management beyond radical orchiectomy. Urology 2017; **107:** 166.
76. Bertolotto M, Boulay-Coletta I, Butini R et al: Imaging of mesothelioma of tunica vaginalis testis. Eur Radiol 2016; **26:** 631.
77. Mensi C, Pellegatta M, Sieno C et al: Mesothelioma of tunica vaginalis testis and asbestos exposure. BJU Int 2012; **110:** 533.
78. Plas E, Riedl CR and Pflüger H: Malignant mesothelioma of the tunica vaginalis testis: review of the literature and assessment of prognostic parameters. Cancer 1998; **83:** 2437.
79. Vogelzang NJ, Rusthoven JJ, Symanowski J et al: Phase III study of pemetrexed in combination with cisplatin versus cisplatin alone in patients with malignant pleural mesothelioma. J Clin Oncol 2003; **21:** 2636.
80. Kondola S, Manners D and Nowak AK: Malignant pleural mesothelioma: an update on diagnosis and treatment options. Ther Adv Respir Dis 2016; **10:** 275.
81. Shahab N and Doll DC: Testicular lymphoma. Semin Oncol 1999; **26:** 259.
82. Koukourakis G and Kouloulias V: Lymphoma of the testis as primary location: tumour review. Clin Transl Oncol 2010; **12:** 321.
83. Deng L, Xu-Monette ZY, Loghavi S et al: Primary testicular diffuse large B-cell lymphoma displays distinct clinical and biological features for treatment failure in rituximab era: a report from the International PTL Consortium. Leukemia 2016; **30:** 361.
84. Brouwer CL, Wiesendanger EM, van der Hulst PC et al: Scrotal irradiation in primary testicular lymphoma: review of the literature and in silico planning comparative study. Int J Radiat Oncol Biol Phys 2013; **85:** 298.
85. Ahmad SS, Idris SF, Follows GA et al: Primary testicular lymphoma. Clin Oncol (R Coll Radiol) 2012; **24:** 358.
86. Vitolo U, Chiappella A, Ferreri AJ et al: First-line treatment for primary testicular diffuse large B-cell lymphoma with rituximab-CHOP, CNS prophylaxis, and contralateral testis irradiation: final results of an international phase II trial. J Clin Oncol 2011; **29:** 2766.
87. Zucca E, Conconi A, Mughal TI et al: Patterns of outcome and prognostic factors in primary large-cell lymphoma of the testis in a survey by the International Extranodal Lymphoma Study Group. J Clin Oncol 2003; **21:** 20.

Study Questions Volume 40 Lesson 35

1. A 21-year-old man has a palpable right scrotal mass. Ultrasound reveals a 3 cm heterogeneous vascular mass in the testicle. Acceptable surgical approaches include
   a. transscrotal percutaneous biopsy for tissue diagnosis
   b. open transscrotal orchiectomy/excision of the mass
   c. orchiectomy via subinguinal incision
   d. orchiectomy via inguinal incision with high ligation of spermatic cord

2. In patients diagnosed with Leydig cell tumors, primary retroperitoneal lymph node dissection (RPLND) can be considered in the setting of one or more pathological predictors of malignancy, which include
   a. absence of necrosis
   b. limited nuclear atypia
   c. primary tumor size greater than 2 cm
   d. greater than 5 mitotic figures per 10 high-power field

3. An 11-year-old boy with a paratesticular rhabdomyosarcoma with no signs of retroperitoneal lymphadenopathy on CT imaging should be managed with
   a. surveillance, perform surgery when lymphadenopathy is observed
   b. bilateral nerve-sparing RPLND
   c. bilateral nerve-sparing RPLND and pelvic lymph node dissection
   d. bilateral nerve-sparing RPLND and inguinal lymph node dissection

4. A 43-year-old man is referred for surgical management of a large left hydrocele. Other than progressing scrotal enlargement limiting activity, the patient is asymptomatic. Examination reveals a normal right testicle and cord structures and a large left hydrocele, limiting examination of the left testicle. The next step is
   a. scrotal support and non-steroidal anti-inflammatory medications as needed.
   b. serum tumor markers
   c. scrotal ultrasound
   d. percutaneous drainage of the hydrocele

5. A 24-year-old man had a 2 cm left testicular mass on physical examination. An ultrasound showed a heterogeneous hypoechoic mass with vascular flow. Serum tumor markers were unremarkable. After a discussion of the treatment options, risks and benefits, the patient underwent an uncomplicated partial orchiectomy revealing an adenomatoid tumor. Following surgery, the management should include
   a. no further followup since the tumor is benign
   b. continued routine self-testicular examination
   c. periodic surveillance ultrasounds
   d. radical orchiectomy

ERRATUM

Telehealth: The New Normal

Volume 40, Lesson 21, Page 205: The disclosures statement for Lesson 21 should read: Chad Ellimoottil: Coloplast: Consultant/Advisor. The online HTML and PDF versions of Lesson 21 have been updated to reflect this change.