Testicular Seminoma and Its Mimics[1]

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Abbreviation: H-E = hematoxylin-eosin

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SA-CME LEARNING OBJECTIVES

After completing this journal-based SA-CME activity, participants will be able to:

- Discuss the pathologic basis for the common imaging features of testicular seminoma.
- List neoplastic and nonneoplastic conditions that may mimic testicular seminoma at imaging.
- Describe the clinical, pathologic, and imaging features that allow distinction of spermatocytic tumor from seminoma.

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Testicular seminoma is the most common malignant tumor of the testis. It classically manifests as a painless mass. Radiologic evaluation with high-frequency ultrasonography (US) is critical for diagnosis. Seminomas are usually homogeneously hypoechoic masses at US. In challenging cases, magnetic resonance (MR) imaging may help confirm that a mass is intratesticular and provide data for local staging. Computed tomography (CT) provides valuable information for staging, including the presence and size of retroperitoneal lymph nodes. Testicular seminoma is treated with radical inguinal orchiectomy and is highly curable even at advanced stages of disease. Several neoplastic and nonneoplastic conditions may mimic testicular seminoma at imaging. Benign mimics include segmental infarction, hematoma, infection, epidermoid cyst, adrenal rests, sarcoidosis, splenogonadal fusion, and sex cord–stromal tumors. Malignant mimics include nonseminomatous germ cell tumors, lymphoma, and metastases. These conditions are individually reviewed with emphasis on features that allow differentiation from seminoma. Spermatocytic tumor, formerly known as spermatocytic seminoma, accounts for only 1% of testicular tumors. It is distinct from classic seminoma, with unique histologic, molecular, and genetic features. It affects an older patient population than classic seminoma and demonstrates indolent clinical behavior. Radiologists serve a key role in diagnosis, staging, and surveillance of patients with seminoma. A thorough knowledge of related clinical, radiologic, and pathologic findings will help the radiologist contribute to high-quality interdisciplinary care of affected patients.

Introduction

Testicular cancer is an important, but curable, medical problem for young men. Testicular seminoma is the most common malignant tumor of the testis. In this article, we discuss testicular seminoma and its mimics with a focus on radiologic-pathologic correlation. Common multimodality imaging findings and important differential considerations are included. We also update the reader on spermatocytic tumor, formerly known as spermatocytic seminoma.

Epidemiology and Risk Factors

Testicular cancer is the most common cancer in men aged 15–44 years (1). Approximately 8720 new cases of testicular cancer were diagnosed in 2016, but only 380 men will die of the disease (2). Although relatively rare, the incidence of testicular germ cell neoplasms has been rising for the past 20 years (1,3,4). In the United States, testicular seminoma is the most common subtype of testicular cancer, accounting for 55% of cases.

TEACHING POINTS

- In the United States, testicular seminoma is the most common subtype of testicular cancer, accounting for 55% of cases.
- It is important to note that testicular seminoma is highly curable even at advanced stages. If all stages of testicular seminoma are included, the 3-, 5-, and 10-year survival rates are 95%, 86%, and 71%, respectively. If a patient presents with stage I disease, the most common stage at presentation, the disease-specific survival is 99%.
- At gray-scale US, seminomas are hypoechoic compared with the background testis. They tend to be homogeneous and may be lobulated or multinodular. Densely echogenic areas or calcifications and cystic spaces are relatively uncommon, seen in 30% and 10%, respectively. At Doppler US, seminoma demonstrates increased vascularity compared with adjacent normal testis.
- A large number of neoplastic and nonneoplastic conditions may mimic testicular seminoma at imaging.
- Until the 2016 update of the World Health Organization (WHO) Classification of Tumours of the Urinary System and Male Genital Organs, spermatocytic tumor was known as spermatocytic seminoma, a subtype of seminoma. Currently, spermatocytic tumor is thought to be unrelated to classic seminoma.

For seminoma, the median age at diagnosis is 35–39 years. On average, seminomas are diagnosed in patients a decade older than those with nonseminomatous germ cell tumors (1). There is significant variability in incidence rates for testicular cancer based on race. White men are at greatest risk, affected five times more often than black men and four times more often than Asian men (5).

Numerous risk factors for testicular cancer have been described in the literature (3,5). The most important of these is a personal history of a testicular germ cell tumor. Patients with a previous germ cell tumor have a 12-fold increased risk of a second testicular primary, a phenomenon that occurs in 2%–3% of patients (5,6). Untreated cryptorchidism increases a patient's chance of developing a testicular neoplasm by eight times (Fig 1). Prepubertal orchiopexy reduces this risk to two times that of the general population.

Family history, combined with environmental factors, increases patients' risk up to 10-fold. Patients with male factor infertility have a threefold increased incidence of testicular cancer. Environmental exposures including organochlorines, polychlorinated biphenyls, polyvinyl chlorides, phthalates, marijuana, and tobacco have been shown to increase the incidence of testicular cancer (3,5). Testicular microlithiasis, a condition that affects approximately 2% of men, was once thought to be a risk factor for testicular cancer. Recent data have failed to show a causal link between this common condition and the much less common testicular cancer (7).

Clinical Features

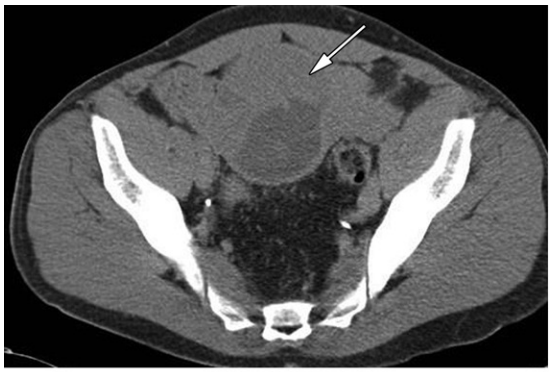
Testicular cancer, including seminoma, classically manifests as a painless, palpable, solid mass. Less commonly, patients with seminoma may present with testicular swelling and mild discomfort, suggestive of epididymo-orchitis (5). After a thorough history and physical examination, most patients are evaluated with scrotal ultrasonography (US) (8). After diagnosis of a solid intratesticular mass, further clinical testing includes complete blood cell count; levels of creatinine, electrolytes, liver enzymes, and serum tumor markers; and chest radiography (3).

The primary therapy for testicular seminoma is radical inguinal orchiectomy (3,9). After surgery, patients are classified into good-, intermediate-, or poor-risk groups according to the International Germ Cell Cancer Collaborative Group classification system (3). This system uses clinically independent prognostic features such as extent of disease and levels of serum tumor markers after orchiectomy (3,10).

If the tumor histologic type is pure seminoma (Fig 2), imaging evaluation includes CT of the abdomen and pelvis to evaluate for retroperitoneal adenopathy. In the presence of retroperitoneal adenopathy or abnormal findings at chest radiography, chest CT is performed to assess for mediastinal adenopathy and detect pulmonary nodules. Magnetic resonance (MR) imaging of the brain and bone scintigraphy are indicated only if symptoms suggestive of metastases to these regions are present (3).

The most commonly used staging system for testicular seminoma is the American Joint Committee on Cancer staging system. Staging of testicular seminoma combines information obtained from pathologic evaluation of the radical orchiectomy specimen (T stage), results of imaging tests (N and M stages), and results of measurement of tumor marker levels (S stage). The inclusion of serum levels of tumor markers (S stage) is unique to testicular cancer. While a detailed discussion of testicular cancer staging is beyond the scope of this article, a few key points are important for radiologists to understand.

The T stage is determined pathologically. Lymph nodes are assessed with imaging and potentially with pathologic analysis. Owing to the lymphatic drainage pathways of the testes, the retroperitoneal lymph nodes are considered the regional lymph nodes. Unlike many other neoplasms, for testicular neoplasm, the greatest dimension of enlarged retroperitoneal lymph nodes is used for staging and should be reported. Key lymph node sizes that alter N staging are less than 2 cm (N1), 2–5 cm (N2), and greater than 5 cm (N3). Initial detection of metastatic disease is



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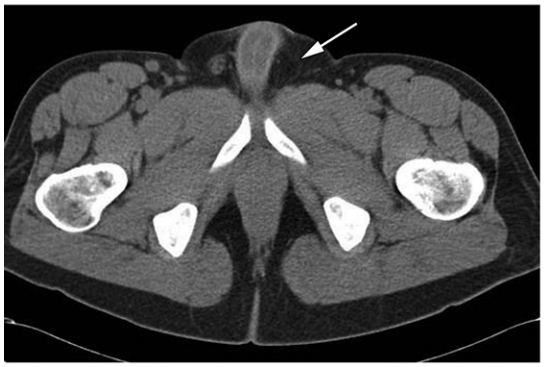

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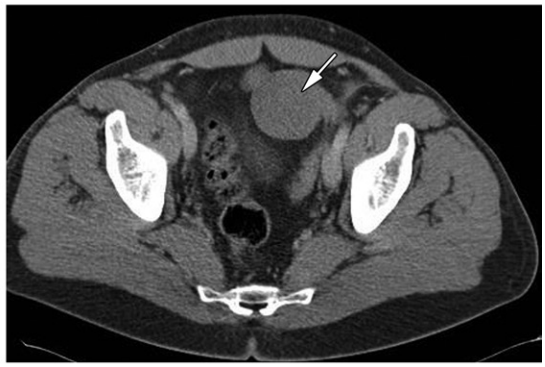

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Figure 1. Cryptorchidism in a 39-year-old man with left flank pain. **(a, b)** Axial contrast-enhanced computed tomographic (CT) images show lack of a left spermatic cord (arrow in **b**) and an anterior pelvic mass (arrow in **a**), proven to be seminoma in an undescended left testis. **(c)** Axial contrast-enhanced CT image 6 months later after chemotherapy shows a reduction in the size of the mass (arrow).

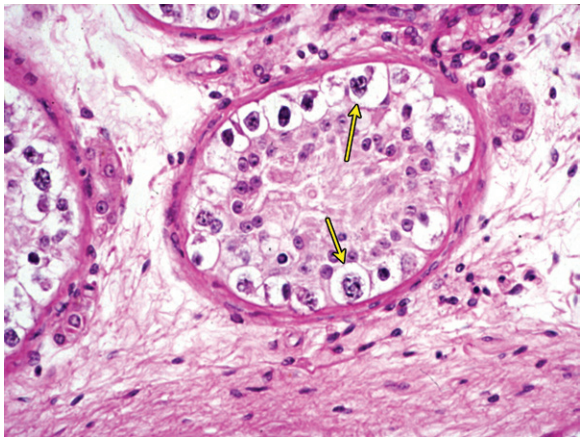


Figure 2. Intratubular seminoma. High-power photomicrograph of a seminiferous tubule shows germ cell neoplasia in situ (GCNIS) (arrows). (Hematoxylin-eosin [H-E] stain.)

usually with imaging. Metastases to nonregional lymph nodes and the lungs are M1a disease, while other distant metastases are considered M1b disease (3,11).

Tumor markers used in management of testicular cancer include α-fetoprotein (AFP), β–human chorionic gonadotropin (β-hCG), and lactate dehydrogenase (LDH) (5,11). AFP levels should be normal in seminoma. When a patient with a histologically pure testicular seminoma has an elevated AFP level, it is generally assumed that an undetected focus of nonseminomatous germ cell tumor is present (3,12). Serum concentrations of β-hCG and LDH may be elevated in patients with seminoma. β-hCG elevation is more commonly seen with nonseminomatous germ cell tumors and other nonneoplastic causes including marijuana use and hypogonadism. LDH is a nonspecific marker of overall tumor burden. Tumor markers may be useful in monitoring metastatic seminomas because elevated tumor marker levels are an early sign of relapse (3).

Adjuvant therapy varies by stage. Stage I pure seminoma may be managed with active surveillance, radiation therapy, or single-agent carboplatin chemotherapy. Radiation therapy is performed for low-volume stage IIA and select stage IIB seminoma. Chemotherapy regimens, including etoposide and cisplatin (EP) or bleomycin, etoposide, and cisplatin (BEP), are used for stage IIB, IIC, and III disease (3) (Fig 1c).

It is important to note that testicular seminoma is highly curable even at advanced stages. If all stages of testicular seminoma are included, the 3-, 5-, and 10-year survival rates are 95%, 86%, and 71%, respectively (13). If a patient presents with stage I disease, the most common stage at presentation, the disease-specific survival is 99% (3,14).

Pathologic Features

An updated World Health Organization (WHO) Classification of Tumours of the Urinary System and Male Genital Organs was published in 2016

(15). Before this update, the classification of testicular tumors was based on morphology alone. Currently, germ cell tumors are divided into two groups, those derived from germ cell neoplasia in situ (GCNIS) and those unrelated to GCNIS. Seminoma is a GCNIS-derived tumor. There may be a transient stage of seminoma that is intratubular (Fig 2). In more than 80% of cases, seminoma shows amplification of genetic material from the short arm of chromosome 12, often in the form of isochromosome 12p (16).

At gross pathologic analysis, classic seminoma is typically tan to pale yellow, solid, and fleshy. It is most often a well-circumscribed mass. Frequently, small foci of hemorrhage and necrosis are present (16). In intertubular seminoma, a distinct mass may not be apparent and instead sporadic irregularities in texture or color are seen (16).

At histologic assessment, seminoma is seen as nests and sheets of cells with intervening thin fibrous septa (Fig 3). The septa separate the tumor into lobules of tumor cells (16). The septa may contain lymphocytes. Seminoma is composed of monotonous cells with clear to pale to eosinophilic cytoplasm. Nuclei are typically large and contain prominent nucleoli. Coexistent granulomatous inflammation may be seen.

In a minority of cases, neoplastic cells may be found in the interstitium of the testis in areas distinct from the main mass, a finding described as intertubular seminoma (17). Intertubular seminoma is frequently associated with GCNIS and is associated with rete testis invasion and a worse prognosis (17). Histologic variants of seminoma include tubular, signet ring, and rhabdoid (16). Syncytiotrophoblasts may be present within the tumor and can be associated with mild elevation of serum β–human chorionic gonadotropin. Seminoma demonstrates immunoreactivity to SALL4, OCT3/4, CKIT, D2-40, and SOX17 (16).

Imaging Features

Ultrasonography

High-frequency US with a linear-array transducer is the initial imaging modality used in evaluation of a suspected testicular mass (8). US is highly accurate in localizing lesions as intratesticular or extratesticular, an important distinction since most intratesticular masses are malignant (18). US is excellent in differentiating benign cysts from more concerning solid or complex masses.

Testicular seminomas are typically unilateral (19). At gray-scale US, seminomas are hypoechoic compared with the background testis (Fig 4). They tend to be homogeneous and may be lobulated or multinodular (19) (Fig 5). Densely echogenic areas or calcifications and cystic spaces are relatively uncommon, seen in 30% and 10%, respectively (20).

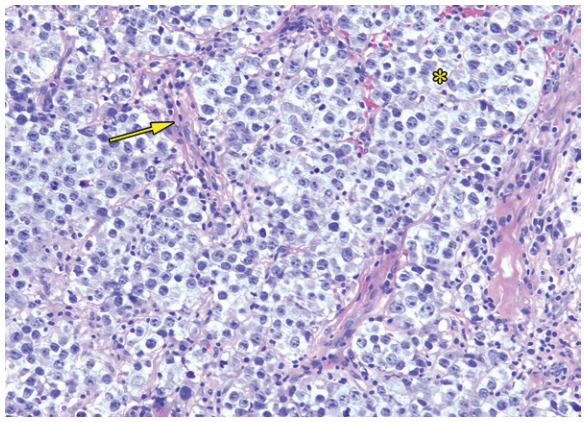


Figure 3. Histologic features of seminoma. High-power photomicrograph of a seminoma shows sheets of monotonous cells with pale cytoplasm and large nuclei (*) with intervening thin fibrous septa (arrow). The uniform appearance of seminoma at histologic analysis helps explain the uniform appearance at imaging. (H-E stain.)

At Doppler US, seminoma demonstrates increased vascularity compared with adjacent normal testis (21). Testicular seminomas are variable in size and in more than 50% of cases may be large enough to replace the entire normal testis (22–24). Sonoelastography reveals increased stiffness in the tumor compared with background normal testis due to the tumor's cellularity and fibrous content (25).

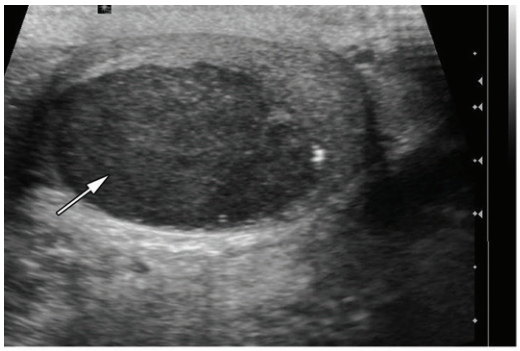
In a small subset of patients with metastatic seminoma, US will demonstrate a normal testicular echotexture without a discrete lesion or only a small lesion or calcification within the testes (26). In the setting of a retroperitoneal mass or bulky adenopathy, the differential diagnosis includes metastatic disease from a "burned-out" testicular tumor or a rare primary retroperitoneal seminoma (23).

Computed Tomography

Approximately 20% of patients have metastatic disease at diagnosis, most commonly to the retroperitoneal lymph nodes. Patients with retroperitoneal adenopathy may present with abdominal or back pain or systemic symptoms (Fig 6) (11). CT may be the first imaging modality in the case of these nonspecific symptoms. Tumors of the right testis typically drain to the interaortocaval nodal group inferior to the renal hilar vessels. Left-sided tumors drain to the para-aortic and preaortic lymph nodes (11). CT is not used in evaluation of the primary testicular lesion.

MR Imaging

Although not routinely performed as part of evaluation of an intratesticular mass, MR imaging has been shown to allow accurate distinction between



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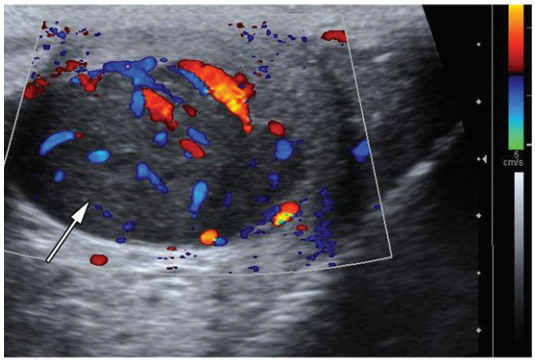

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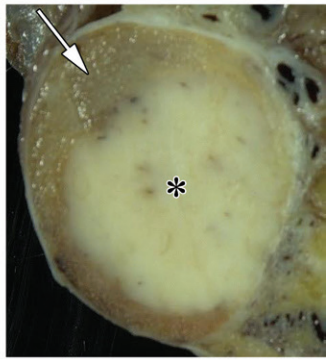

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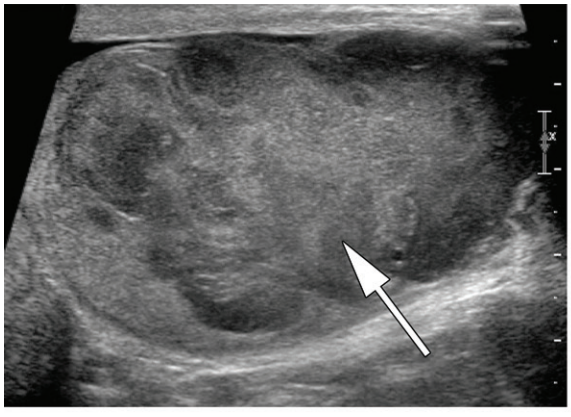
Figure 4. Seminoma in a 27-year-old man with a painless, palpable left testicular mass. **(a, b)** Gray-scale US **(a)** and color Doppler **(b)** images of the left testis show a well-circumscribed hypoechoic mass (arrow in **a**) with marked internal color flow (arrow in **b**), characteristic of seminoma. **(c)** Photograph of the gross pathology specimen shows a tan, fleshy, well-circumscribed mass (*) typical of seminoma and surrounding normal testicle (arrow).



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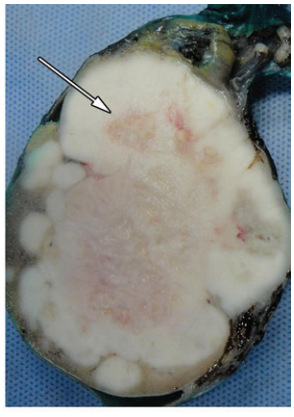


b.

Figure 5. Lobulated seminoma in a 39-year-old man with a painless, palpable left testicular mass. **(a)** Gray-scale US image shows a well-circumscribed, hypoechoic, lobulated mass (arrow) typical of seminoma. **(b)** Photograph of the gross pathology specimen shows a lobulated fleshy mass (arrow) characteristic of seminoma.

seminomatous and nonseminomatous testicular neoplasms (27,28). Seminomas appear as multinodular, sharply defined, homogeneous tumors of low signal intensity on T2-weighted images (27,28). Areas of signal intensity heterogeneity related to hemorrhage or necrosis may be seen.

A key feature in seminoma is visualization of fibrovascular septa, which demonstrate low signal intensity on T2-weighted images and enhance more than the background tumor on postcontrast T1-weighted images. The fibrovascular septa may be thick or thin. A low-signal-intensity halo is variably seen, which correlates with a fibrous capsule at histologic analysis (27).

MR imaging may be used to accurately determine the local extent of disease in testicular carcinoma (29). Although CT is the current imaging test of choice, abdominopelvic MR imaging may also demonstrate retroperitoneal adenopathy and visceral metastases (Fig 6b–6d). MR imaging's lack of ionizing radiation allows a reduction in radiation exposure compared with CT in this young patient cohort with excellent long-term survival rates.

Differential Diagnosis

A large number of neoplastic and nonneoplastic conditions may mimic testicular seminoma at imaging. The following sections review important differential considerations and suggest distinguishing clinical and imaging features (Table).

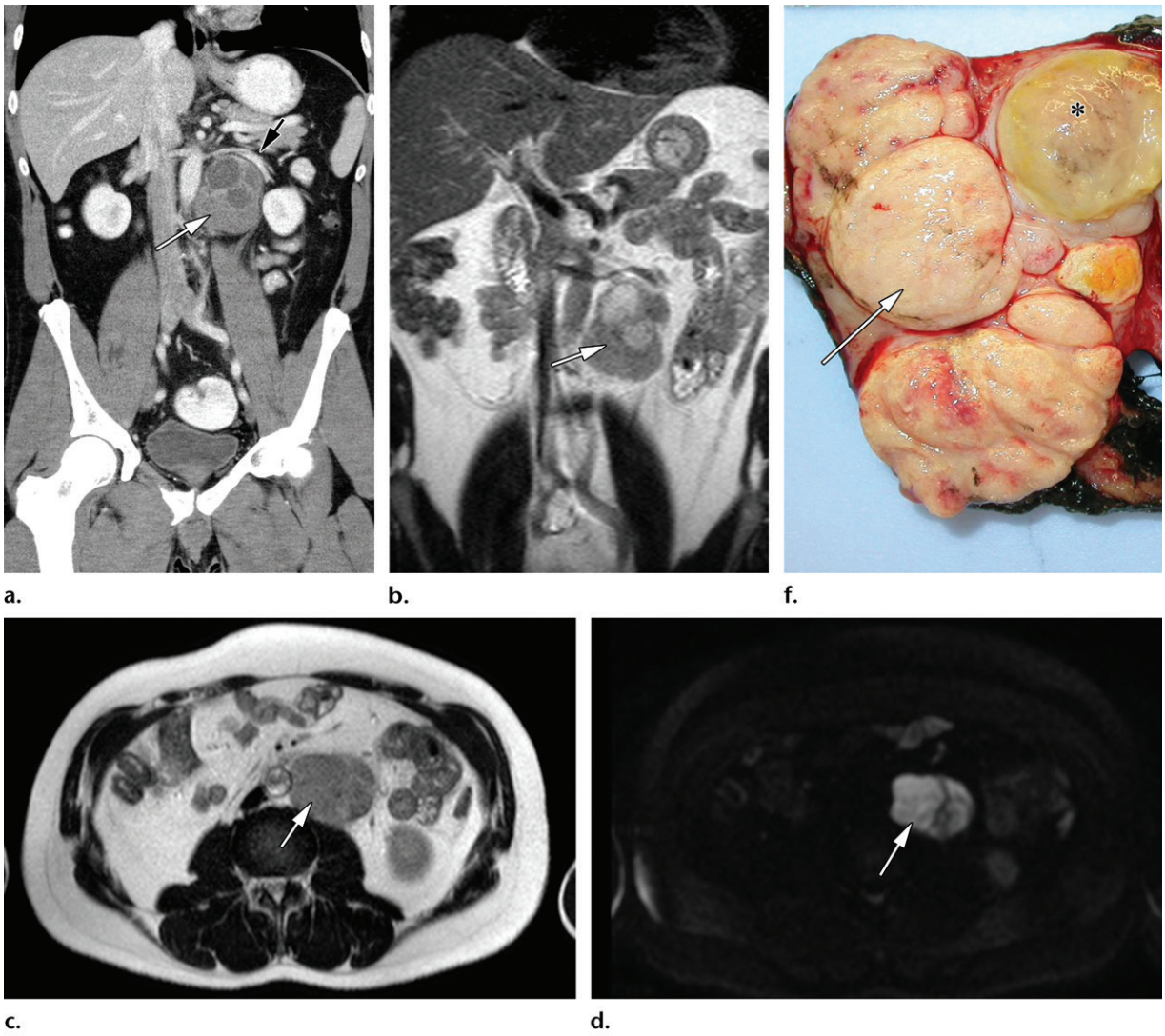


Figure 6. Retroperitoneal adenopathy in a 45-year-old man with left back pain. **(a)** Coronal contrast-enhanced CT image shows left para-aortic adenopathy (white arrow) just below the level of the left renal artery (black arrow). **(b–d)** Coronal T2-weighted single-shot fast spin-echo (SSFSE) **(b)**, axial T2-weighted SSFSE **(c)**, and axial diffusion-weighted **(d)** MR images show the retroperitoneal adenopathy (arrow in **b** and **c**) with restricted diffusion (arrow in **d**). **(e)** Gray-scale US image obtained to look for a primary malignancy shows a well-circumscribed hypoechoic mass (arrow) representing primary testicular seminoma. **(f)** Photograph of the gross pathology specimen shows the retroperitoneal adenopathy with cystic space seen at imaging (*) and a solid, tan, fleshy, well-circumscribed mass (arrow) characteristic of seminoma.

Benign Lesions

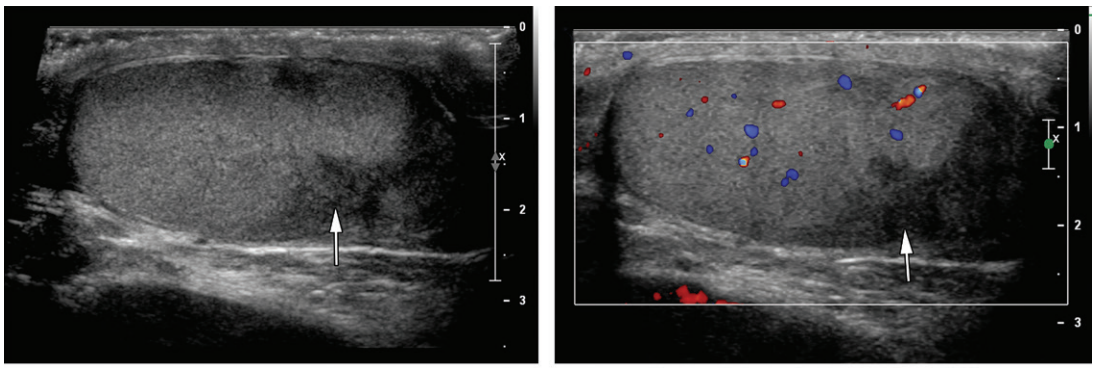
Segmental Infarction

Segmental infarction is an uncommon condition that may be idiopathic or represent a complication of epididymo-orchitis, prior testicular torsion, sickle cell anemia, vasculitis, or other hypercoagulable states (30,31). In cases of segmental infarction due to epididymo-orchitis, it has been suggested that venous compromise can result in a rounded lesion (30). The median age of patients with segmental infarction is 37 years, which overlaps with the age of the population that develops testicular seminoma.

At US, segmental infarction appears as a wedge-shaped or rounded area of hypoechogenicity within either testis (32) (Fig 7). When the lesion is wedge shaped, its apex is located at the mediastinum testis. When the area of infarction is rounded and homogeneous, it may mimic seminoma. A helpful US feature to distinguish

Key Clinical and Imaging Features of Mimics of Testicular Seminoma

Mimics	Distinguishing Features: Clinical	Distinguishing Features: Imaging
Benign		
Segmental infarction	Painful	Wedge-shaped Hypo- or avascular
Testicular hematoma	Recent trauma	Evolution over time becoming smaller and more hypoechoic Avascular
Testicular infection (orchitis)	Resolution with antibiotic therapy	Evidence of concomitant epididymitis including edema and hyperemia of ipsilateral epididymis, reactive hydrocele or pyocele, and scrotal edema
Epidermoid cyst	None	Characteristic "onion ring" appearance Avascular
Adrenal rests	History of congenital adrenal hyperplasia	Commonly bilateral
Sarcoidosis	Demographics: more common in black men	Concomitant thoracic findings of sarcoidosis including perilymphatic nodules and mediastinal and hilar lymphadenopathy
Splenogonadal fusion	None	Central vascular pattern with vessels branching to periphery Positive findings on technetium 99m (^{99m}Tc) sulfur colloid scans
Sex cord–stromal tumors	Demographics: younger patient population Hormone-related symptoms: precocious puberty or gynecomastia	None
Malignant		
Nonseminomatous germ cell tumors	Demographics: younger patient population (overlap exists)	Heterogeneous appearance with cystic spaces and calcifications Ill-defined margins
Lymphoma	Demographics: patient age > 60 years	Higher frequency of bilateral tumors
Metastases	Demographics: older patient population Known primary malignancy, especially prostate carcinoma	Higher frequency of bilateral tumors



a. **b.**

Figure 7. Testicular infarct in a 35-year-old man with a history of left epididymitis-orchitis. Gray-scale US **(a)** and color Doppler **(b)** images of the left testis show a wedge-shaped hypoechoic region (arrow in **a**) without internal vascular flow (arrow in **b**), compatible with segmental infarction.

segmental infarction from seminoma is markedly decreased or absent vascular flow at Doppler imaging (32). Clinically, segmental infarction typically manifests as acute pain, unlike the classic presentation of seminoma as a painless mass (30).

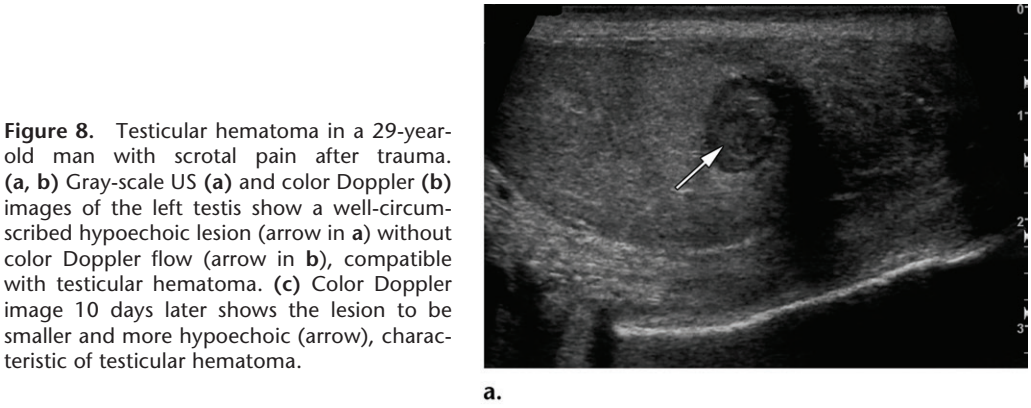


Figure 8. Testicular hematoma in a 29-year-old man with scrotal pain after trauma. **(a, b)** Gray-scale US **(a)** and color Doppler **(b)** images of the left testis show a well-circumscribed hypoechoic lesion (arrow in **a**) without color Doppler flow (arrow in **b**), compatible with testicular hematoma. **(c)** Color Doppler image 10 days later shows the lesion to be smaller and more hypoechoic (arrow), characteristic of testicular hematoma.

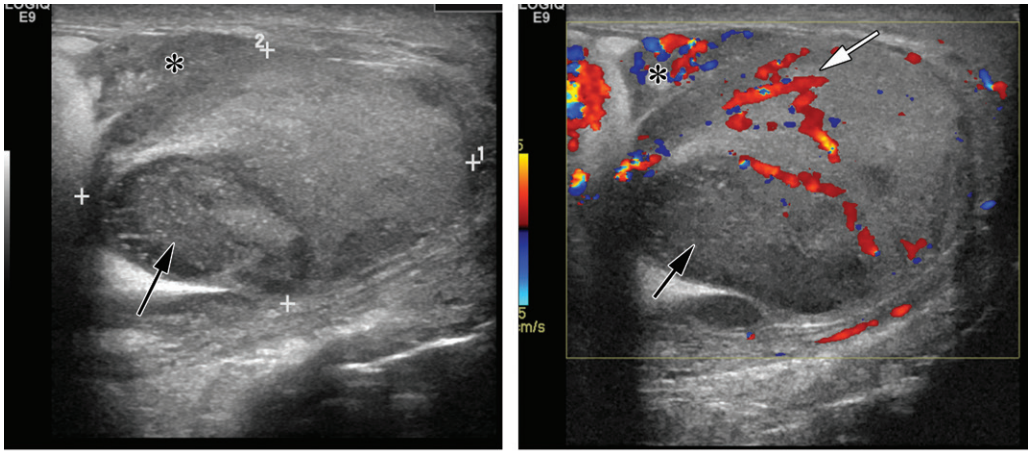


Figure 9. Epididymitis-orchitis with abscess in a 40-year-old man with a 2-week history of right scrotal pain. Gray-scale US **(a)** and color Doppler **(b)** images of the right testis show an enlarged hyperemic epididymis (* in **a** and **b**) and increased testicular flow (white arrow in **b**). A focal area of decreased echogenicity (arrow in **a**) with no internal flow (black arrow in **b**) represents an intratesticular abscess.

Testicular Hematoma

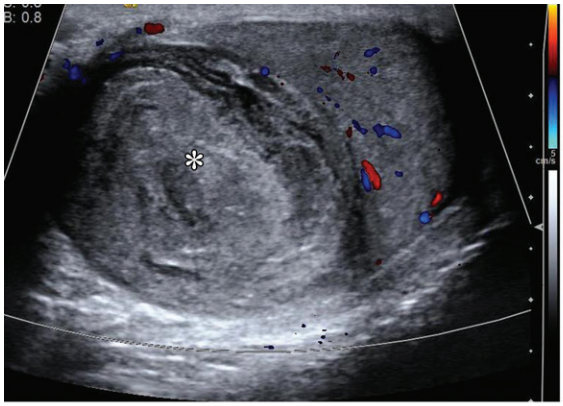
Testicular hematomas are a common consequence of testicular trauma. The US appearance of a testicular hematoma evolves over time (33). Acutely, hematomas are iso- to hyperechoic. Over time, hematomas decrease in size and become progressively more hypoechoic (33) (Fig 8).

Depending on the interval between the traumatic event and the imaging assessment, there may be overlap in the imaging findings of hematoma and seminoma. Fortunately, at Doppler evaluation hematomas are avascular, a helpful distinguishing feature from seminoma (34). If there is concern about an incidental testicular tumor discovered at testicular US performed for trauma, follow-up imaging to ensure resolution should be performed.

Testicular infection

Testicular infection, including orchitis with or without abscess formation, may mimic seminoma. In the acute phase of orchitis, diffuse testicular edema results in a hypoechoic appearance of the testis

Figure 10. Epidermoid cyst in a 45-year-old man with a painless, palpable right testicular mass. **(a)** Gray-scale US image of the right testis shows a well-circumscribed hypoechoic mass with an "onion skin" appearance (*), classic for epidermoid cyst. **(b, c)** Photograph of the gross pathology specimen **(b)** and low-power photomicrograph **(c)** show the characteristic keratinous material with a laminated appearance (* in **b**, black * in **c**). The cyst is lined by keratinizing squamous epithelium (white * in **c**). (H-E stain.)



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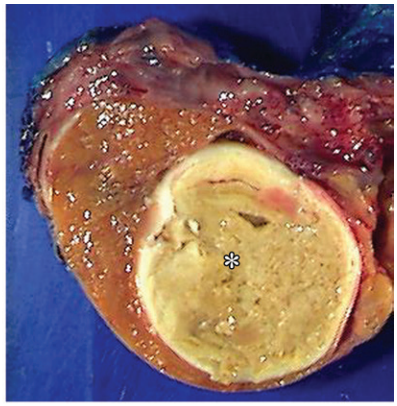

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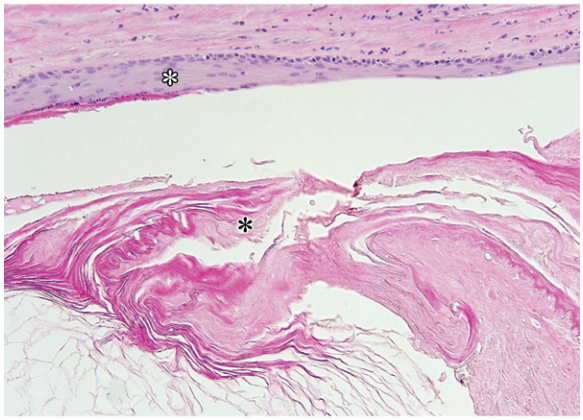


c.

(35). As the infection and inflammation evolve, the regions of hypoechogenicity become more localized (36). Since seminoma may appear as focal, multinodular, or diffuse regions of hypoechogenicity, the gray-scale US appearance may overlap. Furthermore, both orchitis and seminoma result in increased vascularity at Doppler imaging (35) (Fig 9).

Helpful imaging findings to suggest orchitis over seminoma include edema and hypervascularity of the ipsilateral epididymis, reactive hydrocele or pyocele, and associated scrotal edema (36). These findings are uncommon in seminoma. Clinically, seminoma may manifest with signs and symptoms that mimic orchitis. If doubt exists after the initial imaging assessment, follow-up imaging after a course of antibiotics should be performed.

Epidermoid Cyst

Epidermoid cysts, which account for 1% of testicular lesions, are composed of keratinizing, stratified, squamous epithelium surrounded by a fibrous wall (37). At US, epidermoid cysts are well-defined rounded lesions with a characteristic "onion ring" internal pattern of echoes (38) (Fig 10). Although these lesions are cystic, they may mimic an avascular or hypovascular solid lesion due to their internal echoes. When the characteristic imaging findings are present, this lesion should be distinguishable from the homogeneously hypoechoic appearance of seminoma (19).

Adrenal Rests

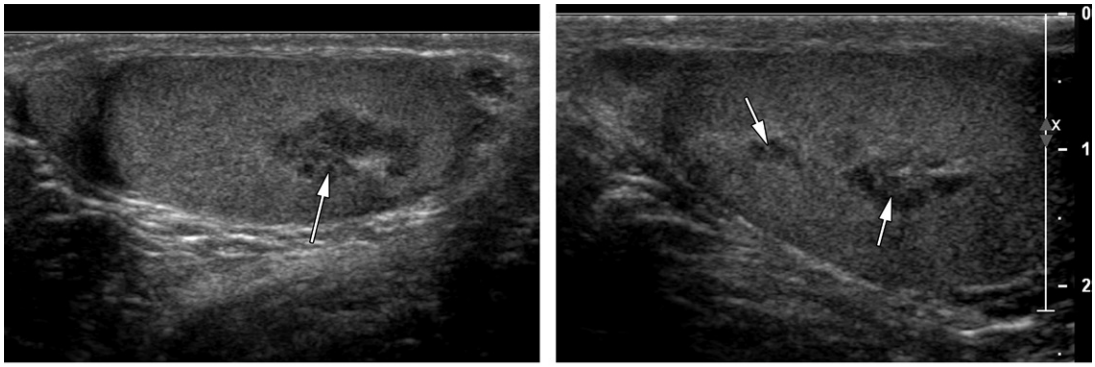
Adrenal rests commonly affect patients with congenital adrenal hyperplasia (CAH), a heterogeneous group of autosomal recessive genetic conditions (39). Patients with CAH have enzymatic defects that result in inadequate cortisol production. Owing to a lack of negative feedback, patients produce excess corticotropin, which may result in hypertrophy of ectopic adrenal cells within otherwise normal testes.

At US, adrenal rests are commonly hypoechoic masses, similar to seminoma (40). They can be variable in size, with one recent series describing a range of 4–38 mm (39). Adrenal rests are usually bilateral, an uncommon occurrence in seminoma (Fig 11). Although the imaging features of seminoma and adrenal rests may overlap, the clinical history should make differentiation possible. Additionally, alterations in treatment focused on reducing excess corticotropin may cause the lesions to regress at follow-up imaging (39).

Sarcoidosis

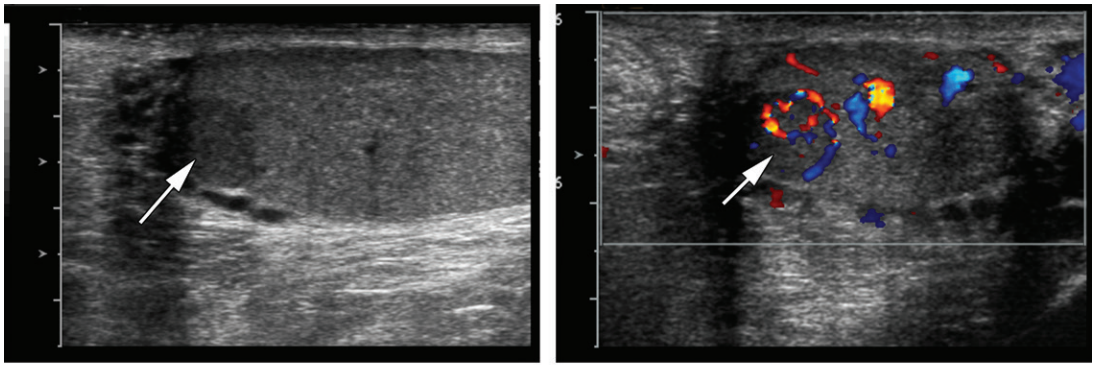
Sarcoidosis is a systemic disease characterized by formation of noncaseating granulomas. Involvement of the testis in systemic sarcoidosis is uncommon, affecting approximately 4% of patients (41). The clinical presentation is variable, ranging from an asymptomatic incidental finding to acute testicular pain. At US, testicular sarcoidosis is

Figure 11. Adrenal rests in a 25-year-old man with known congenital adrenal hyperplasia who presented with rising laboratory values despite treatment. Gray-scale US images of the right **(a)** and left **(b)** testes show bilateral hypoechoic masses (arrows) representing adrenal rests.

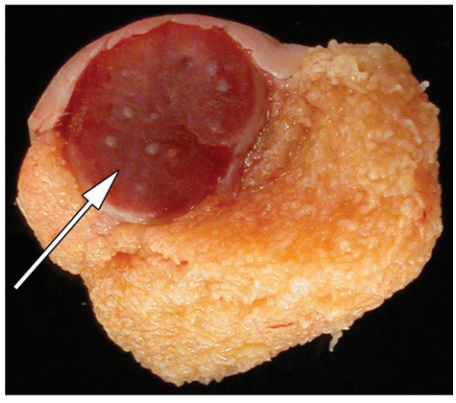


a. **b.**

Figure 12. Splenogonadal fusion in a 29-year-old man with a painless, palpable left testicular mass, found during workup for infertility. **(a, b)** Gray-scale US **(a)** and color Doppler **(b)** images of the left testis show a hypoechoic mass (arrow in **a**) with internal flow (arrow in **b**). **(c)** Photograph of the gross pathology specimen shows a mass (arrow) representing splenic tissue.



a. **b.**



c.

most commonly a focal hypoechoic mass lesion, similar to seminoma (41,42).

Clinical factors may allow differentiation of sarcoidosis from seminoma. Since isolated testicular involvement is rare, the presence of characteristic findings of pulmonary sarcoidosis may help, although mediastinal adenopathy can be seen with both conditions. Epidemiology may also be helpful, as seminoma commonly affects white men while sarcoidosis more frequently affects black men (42).

Splenogonadal Fusion

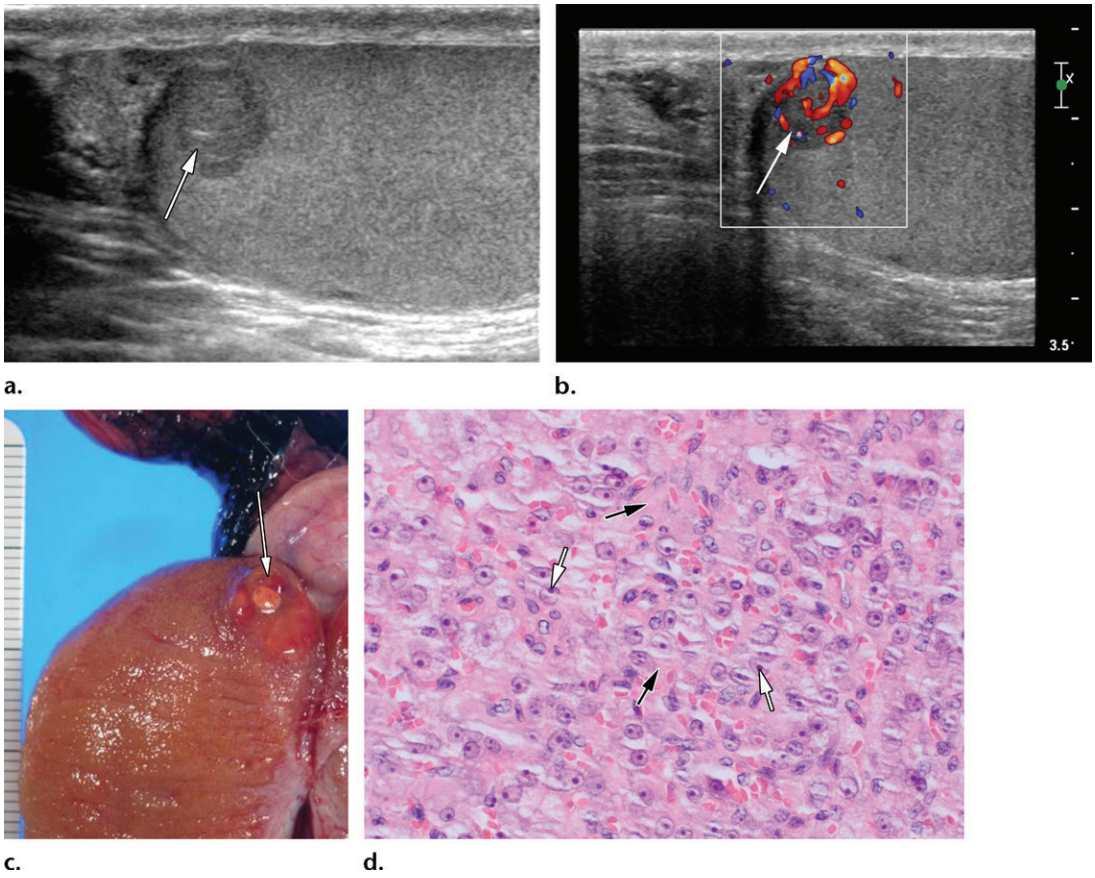
Splenogonadal fusion is a rare condition that involves congenital fusion of the testis with ectopic splenic tissue (43). Splenogonadal fusion is associated with cryptorchidism, also a risk factor for seminoma (43). Patients most commonly present with a painless mass, the most common presentation of seminoma.

The ectopic splenic tissue is usually hypoechoic at gray-scale US and may be challenging to separate from the ipsilateral testis (41,43) (Fig 12). It has been suggested that a central vascular pattern with vessels branching toward the lesion's periphery may be a helpful distinguishing feature (41). If splenogonadal fusion is suspected, ^{99m}Tc sulfur colloid scans can confirm activity in ectopic splenic tissue (44).

Sex Cord–Stromal Tumors

Sex cord–stromal tumors, including Leydig cell tumor, Sertoli cell tumor, thecoma, and

Figure 13. Leydig cell neoplasm in a 24-year-old man with a palpable right scrotal mass and new-onset gynecomastia. **(a, b)** Gray-scale US **(a)** and color Doppler **(b)** images of the right testis show a well-circumscribed hypoechoic mass (arrow in **a**) with internal color flow (arrow in **b**). **(c, d)** Photograph of the gross pathology specimen **(c)** and high-power photomicrograph **(d)** show a well-circumscribed mahogany brown mass (arrow in **c**) and polygonal cells with abundant eosinophilic cytoplasm (black arrows in **d**) and prominent nucleoli (white arrows in **d**), characteristic of Leydig cell tumor. (H-E stain.)



granulosa cell tumor, are uncommon testicular neoplasms, accounting for only 5% of testicular neoplasms (23). Sex cord–stromal tumors are typically benign, although malignant cases have been reported. At US, sex cord–stromal tumors may appear as a focal hypoechoic mass, identical to seminoma (Fig 13). Distinguishing clinical features are young age at presentation and hormone-related symptoms, such as precocious puberty or gynecomastia (24).

Malignant Lesions

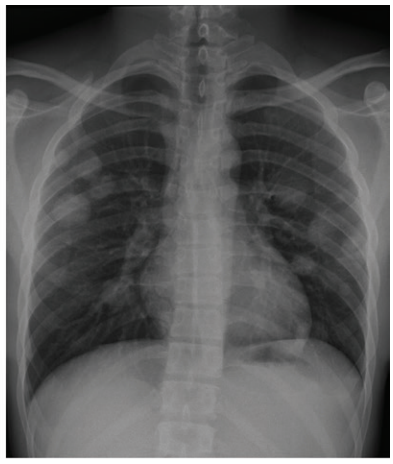
Nonseminomatous Germ Cell Tumors

Nonseminomatous germ cell tumors include embryonal carcinoma, teratoma, yolk sac tumor, and choriocarcinoma (3). The most common nonseminomatous germ cell tumor is mixed germ cell tumor (MGCT), where multiple histologic subtypes coexist (19). MGCTs tend to be more heterogeneous in echotexture and echogenicity than seminomas.

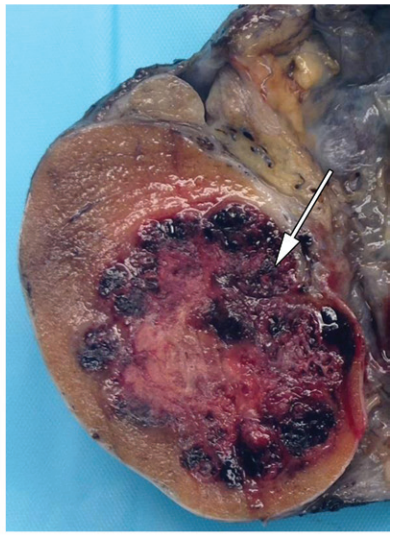
Although seminomas, especially large seminomas, may demonstrate cystic spaces and calcifications, these findings are more commonly encountered in MGCT (Fig 14). MGCTs are more likely to have ill-defined margins than are seminomas (24). The clinical presentations of seminomatous and nonseminomatous tumors overlap, but on average men with seminoma tend to be about a decade older than patients with nonseminomatous tumors (23).

Lymphoma

Non-Hodgkin B-cell lymphoma is the most common testicular malignancy in men older than 60 years (45). At US, testicular lymphoma is hypoechoic and hypervascular, similar to both seminoma and epididymo-orchitis (46) (Fig 15). Testicular lymphoma is typically painless, allowing clinical differentiation from epididymo-orchitis. Lymphoma is usually unilateral but can be bilateral in approximately one-third of cases, a much higher percentage than seminoma. Although the imaging appearance of lymphoma parallels that of seminoma, the affected patient population is significantly older (23).



a.



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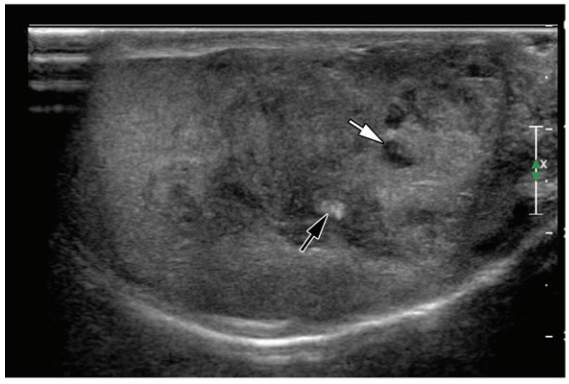


b.

Figure 14. Malignant MGCT in a 20-year-old man with left chest pain. **(a)** Posteroanterior chest radiograph shows pulmonary metastases. Testicular US was performed to look for a primary neoplasm. **(b)** Gray-scale US image of the left testis shows an ill-defined heterogeneous mass with cystic spaces (white arrow) and calcifications (black arrow). **(c)** Photograph of the gross pathology specimen shows a variegated appearance (arrow) secondary to the heterogeneity of the tumor, which explains the heterogeneous US appearance.

Metastases

Although uncommon, a variety of primary tumors can metastasize to the testes. The most common primary malignancy that spreads to the testis is prostate adenocarcinoma, accounting for 35% of cases (24). Metastases due to tumors of the lung, skin (melanoma), colon, and kidney have also been described (24). The imaging appearance of testicular metastases is nonspecific and may overlap with that of seminoma.

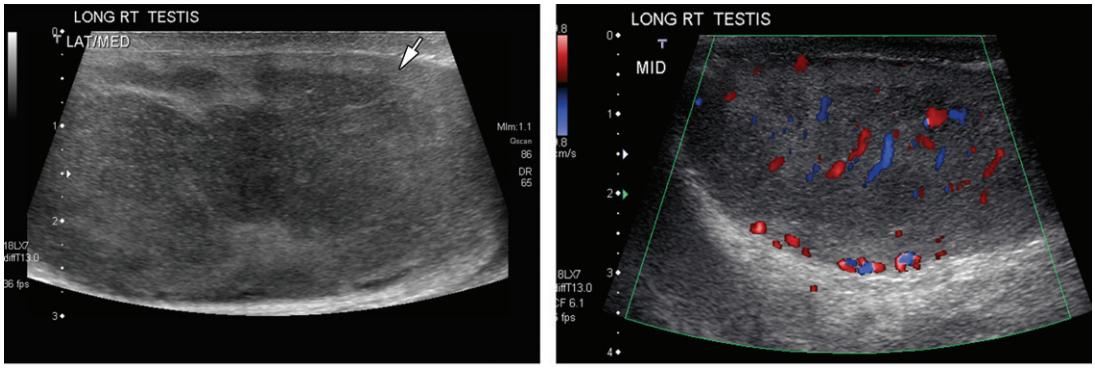
Fortunately, epidemiologic factors may help. Patients affected by testicular metastases are older on average than men with seminoma. Testicular metastases usually occur in the setting of advanced metastatic disease. Additionally, most metastases are unilateral, but bilateral disease can be seen in up to 15% of patients (23).

Spermatocytic Tumor

Until the 2016 update of the World Health Organization (WHO) Classification of Tumours of the Urinary System and Male Genital Organs (15), spermatocytic tumor was known as spermatocytic seminoma, a subtype of seminoma. Currently, spermatocytic tumor is thought to be unrelated to classic seminoma (15). Specifically, spermatocytic tumor lacks an association with germ cell neoplasia in situ (GCNIS). It also lacks 12p amplification and shows a unique amplification of chromosome 9 corresponding to the *DMRT1* gene (15). Spermatocytic tumor is not associated with cryptorchidism, a major risk factor for seminoma (47).

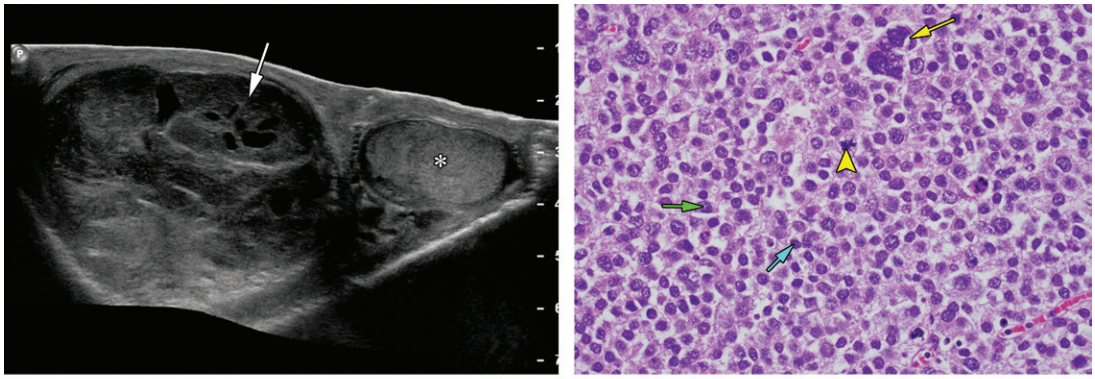
Spermatocytic tumor accounts for only 1% of testicular cancers. It affects older men than does classic seminoma, with a median age at diagnosis of 54 years (1). It is unilateral in 90% of cases, but at 10%, bilateral disease is more common than in classic seminoma (48).

Spermatocytic tumor manifests as a slowly enlarging but painless mass. The majority of tumors are larger than 5 cm at diagnosis. It demonstrates indolent behavior, rarely metastasizing in the absence of sarcomatous transformation. Coexistent sarcoma occurs in 6% of cases (47).

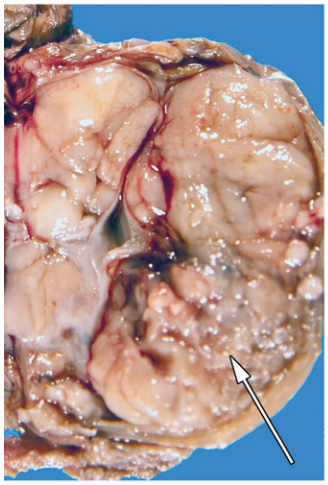


a. b.

Figure 15. Lymphoma in a 72-year-old man with right testicular pain and swelling. Gray-scale US **(a)** and color Doppler **(b)** images of the right testis show an ill-defined, hypoechoic, hypervascular mass replacing almost the entire testis, which was proven to be diffuse large B-cell lymphoma. Note the remaining rim of normal testicular tissue (arrow in **a**).



a. c.



b.

Figure 16. Spermatocytic tumor in an 85-year-old man with an enlarging, painless right testicular mass. **(a)** Panoramic gray-scale US image shows a markedly enlarged heterogeneous right testis (arrow) adjacent to the normal left testis (*). **(b)** Photograph of the gross pathology specimen shows the heterogeneous appearance of the tumor (arrow). **(c)** High-power photomicrograph shows the characteristic small cells (blue arrow), intermediate cells (green arrow), and giant cells (yellow arrow) of spermatocytic tumor. The intermediate cells show a spireme-like chromatin distribution. Mitoses (arrowhead) are also present. (H-E stain.)

The typical therapy for spermatocytic tumor without sarcomatous transformation is limited to curative orchiectomy.

Despite the disparate molecular features of seminoma and spermatocytic tumor, the gross features are similar. Exceptions include a more gelatinous appearance of the cut tumor surface and more cystic spaces in spermatocytic tumor than in seminoma (16).

At histologic analysis, spermatocytic tumor is composed of an admixture of small, medium, and giant tumor cells (Fig 16). The giant cells may be multinucleate. Pleomorphism, atypical mitoses, and apoptosis are common findings (16). The tumor cells lack the glycogenation seen in seminoma. At immunohistochemical staining, SALL4 shows positivity. CKIT is positive in 50% of cases. Spermatocytic tumor does not react to OCT3/4 (16).

Only limited descriptions of the US appearance of spermatocytic tumor are present in the literature (48). These reports describe spermatocytic tumor as a well-defined but inhomogeneous mass (47). It may contain cystic spaces (48).

Conclusion

Testicular cancer, of which seminoma is the most common pure subtype, is an important disease affecting young men. Radiologists have a vital role in diagnosis, staging, and follow-up of patients

affected by seminoma. A thorough understanding of the clinical, radiologic, and pathologic findings of this disease will help the radiologist contribute to high-quality interdisciplinary care of affected patients. With adherence to current diagnostic and treatment protocols, long-term survival of patients with testicular seminoma can be achieved.

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