Retroperitoneal Leiomyosarcoma

Jamie Marko, MD
Darcy J. Wolfman, MD

Abbreviations: ADC = apparent diffusion coefficient, AFP = α-fetoprotein, β-hCG = β–human chorionic gonadotropin, FNCLCC = Federation Nationale des Centres de Lutte Contre le Cancer, H-E = hematoxylin-eosin, IgG4 = immunoglobulin G4, IVC = inferior vena cava, LDH = lactate dehydrogenase, SDH = succinate dehydrogenase, SMA = smooth muscle actin, SSFSE = single-shot fast spin-echo

RadioGraphics 2018; 38:1403–1420

https://doi.org/10.1148/rg.2018180006

Content Codes: CT GU MR OI

From the Department of Radiology and Imaging Sciences, National Institutes of Health, Bethesda, Md (J.M.); American Institute for Radiologic Pathology, 1100 Wayne Ave, Suite 1020, Silver Spring, MD 20910 (J.M., D.J.W.); and Community Radiology Division, Johns Hopkins School of Medicine, Washington, DC (D.J.W.). Received January 1, 2018; revision requested March 28 and received April 21; accepted April 26. For this journal-based SA-CME activity, the authors, editor, and reviewers have disclosed no relevant relationships. **Address correspondence to** D.J.W. (e-mail: *darcywolfman@gmail.com*).

Supported by the American Institute for Radiologic Pathology, the Joint Pathology Center, and Uniformed Services University of the Health Sciences. The views expressed in this article are those of the authors and do not necessarily reflect the official policy or position of the Department of Defense or the U.S. Government.

SA-CME LEARNING OBJECTIVES

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

- Describe the pathologic findings most commonly seen with retroperitoneal leiomyosarcoma.
- List the three patterns of growth of retroperitoneal leiomyosarcoma.
- Describe the most common imaging features of retroperitoneal leiomyosarcoma.

See rsna.org/learning-center-rg.

Leiomyosarcoma is a malignant neoplasm that shows smooth muscle differentiation. It is the second most common sarcoma to affect the retroperitoneum. Retroperitoneal leiomyosarcomas may grow to large sizes before detection and may be an incidental finding at imaging. When symptomatic, retroperitoneal leiomyosarcoma may cause compressive symptoms, including pain. Retroperitoneal leiomyosarcoma most commonly manifests as a large soft-tissue mass, with areas of necrosis. The most frequent pattern of growth is an entirely extravascular mass. Less commonly, leiomyosarcoma may demonstrate both extravascular and intravascular components. Rarely, retroperitoneal leiomyosarcomas are completely intravascular, typically arising from the inferior vena cava. Given its variable imaging features, a large variety of neoplastic and nonneoplastic conditions are included in the differential diagnosis of retroperitoneal leiomyosarcoma. In this review, the authors discuss retroperitoneal leiomyosarcoma, with emphasis on the pathologic basis of disease, and illustrate the multimodality imaging appearances of retroperitoneal leiomyosarcoma using cases from the Radiologic Pathology Archives of the American Institute for Radiologic Pathology. The authors review important differential considerations of retroperitoneal leiomyosarcoma, focusing on the extravascular pattern of growth, and emphasize clinical and imaging features that help radiologists differentiate leiomyosarcoma from the most frequent mimics. The information presented in this review will aid radiologists in fulfilling their key roles in the diagnosis, operative planning, and follow-up of patients with retroperitoneal leiomyosarcoma.

Introduction

Leiomyosarcoma is a malignant neoplasm that shows smooth muscle differentiation (1). Although soft-tissue sarcomas including leiomyosarcoma can occur in a myriad of anatomic locations, the retroperitoneum is a common site of origin, accounting for 12%–69% of cases (2,3). Radiologic imaging is important in the diagnosis, operative planning, and follow-up of patients with retroperitoneal leiomyosarcoma.

TEACHING POINTS

- Leiomyosarcoma is the second most common subtype of retroperitoneal soft-tissue sarcoma, accounting for 28% of cases. Leiomyosarcoma is the most common sarcoma to arise from the large blood vessels in the retroperitoneum, including the IVC and renal veins.
- Because of their retroperitoneal location and the relative sparing of visceral structures, retroperitoneal leiomyosarcomas may grow to large sizes before detection and are commonly an incidental finding at imaging.
- The key histologic criteria used to diagnose leiomyosarcoma in the retroperitoneum include at least one of the following: cellular pleomorphism or atypia, coagulative tumor cell necrosis, and more than 10 mitotic figures per 50 high-powered fields (HPFs) in women or more than one mitotic figure per 50 HPFs in men.
- Retroperitoneal leiomyosarcomas classically appear as large soft-tissue masses, often with areas of necrosis, hemorrhage, or cystic change. Calcifications are uncommon, except in rare cases of osteosarcomatous differentiation.
- Radiologic imaging plays a key role in determining the possibility of surgical resection, given its ability to determine the mass's precise anatomic relationship to key retroperitoneal organs and major vascular structures. Imaging also helps detect metastases in a large number of cases, altering the patient's prognosis and treatment options.

In this review, we discuss retroperitoneal leiomyosarcoma with emphasis on the pathologic basis of disease. We illustrate the multimodality imaging appearances of retroperitoneal leiomyosarcoma and highlight important differential considerations. Given the broad range of conditions that affect the retroperitoneum, we focus our discussion on the differential diagnosis of potential mimics of extravascular leiomyosarcoma, the most commonly encountered subtype. The differential diagnosis includes both benign and malignant neoplasms, as well as nonneoplastic conditions that can appear masslike (Table). We emphasize their distinguishing clinical and imaging features.

Epidemiology

Soft-tissue sarcomas are an important group of retroperitoneal neoplasms. Leiomyosarcoma is the second most common subtype of retroperitoneal soft-tissue sarcoma, accounting for 28% of cases (4). Leiomyosarcoma is the most common sarcoma to arise from the large blood vessels in the retroperitoneum, including the inferior vena cava (IVC) and renal veins. Retroperitoneal leiomyosarcomas are most commonly diagnosed in patients between 54 and 65 years of age but can uncommonly affect children (5,6). Women are more commonly affected than men, with leiomyosarcomas with IVC involvement occurring five times more commonly in women than in men (1,7).

Clinical Features

Retroperitoneal leiomyosarcomas typically manifest as large soft-tissue masses. Because of their retroperitoneal location and the relative sparing of visceral structures, retroperitoneal leiomyosarcomas may grow to large sizes before detection and are commonly an incidental finding at imaging (8). When symptomatic, retroperitoneal leiomyosarcomas may cause compressive symptoms, including pain.

Approximately 38% of retroperitoneal leiomyosarcomas have an intraluminal component (4). Leiomyosarcomas with substantial intraluminal components manifest earlier than extraluminal leiomyosarcomas because they are more often symptomatic (9). The signs and symptoms associated with leiomyosarcoma of the IVC vary by the tumor's location in the IVC. If the suprahepatic IVC is involved, the mass can obstruct the hepatic veins and cause Budd-Chiari syndrome. Signs of Budd-Chiari syndrome include hepatomegaly, jaundice, and ascites. If the mass is located in the mid-IVC, it may obstruct the renal veins, leading to renal dysfunction. Involvement of the infrarenal IVC can lead to leg edema (1).

Pathologic Features

Gross Pathology

Leiomyosarcomas are fleshy masses that may be gray, white, or tan. The mass may have a whorled appearance. Large tumors often show hemorrhage, necrosis, or cystic change (Figs 1, 2). The mass usually has a well-circumscribed margin but can appear infiltrative on occasion (1).

Histopathology

Retroperitoneal leiomyosarcomas arise from smooth muscle tissue located in the retroperitoneum or the walls of the large retroperitoneal veins (10). Important pathologic differential considerations for spindle cell neoplasms in the retroperitoneum include benign leiomyoma and smooth muscle tumor of uncertain malignant potential. The key histologic criteria used to diagnose leiomyosarcoma in the retroperitoneum include at least one of the following: cellular pleomorphism or atypia, coagulative tumor cell necrosis, and more than 10 mitotic figures per 50 high-powered fields (HPFs) in women or more than one mitotic figure per 50 HPFs in men (11,12).

The typical microscopic pattern of disease seen in leiomyosarcoma is intersecting sharply marginated fascicles of spindle cells (Figs 2–4). Occasionally, a focal storiform, palisaded, or hemangiopericytoma–like arrangement may manifest. Leiomyosarcomas are usually compactly cellular, but fibrosis or myxoid change may

Key Clinical and Imaging Features Used in the Differential Diagnosis of Retroperitoneal Leiomyosarcoma

Diagnosis	Clinical Features	Imaging Features
Lymphoma	Presence of B symptoms Elevated lactate dehydrogenase (LDH) level	Well-defined margins No necrosis or calcification without treatment Mild homogeneous enhancement No vascular invasion
Metastases	History of primary malignancy	Imaging evidence of a primary mass Metastases, especially to the lymph nodes
Liposarcoma	None	Macroscopic fat Calcifications
Neurofibroma	History of neurofibromatosis Younger male patients (20–40 years)	Homogeneous Hypoattenuating at CT Uniform enhancement Target appearance at T2-weighted MRI Dumbbell shape
Schwannoma	Young to middle-aged patients (20–50 years)	Paraspinal or presacral location Homogeneous and round when small Calcifications Lack of vascular involvement
Ganglioneuroma	Children to young adults	Paraspinal location Hypoattenuating with mild enhancement Calcifications Lack of necrosis or hemorrhage
Paraganglioma	Young patient Predisposing condition such as neurofibromatosis type 1, multiple endocrine neoplasia syndrome 2, von Hippel–Lindau syndrome, or Carney's triad Predisposing genetic mutation (ie, succinate dehydrogenase [SDH] genes)	Located at organ of Zuckerkandal Intense enhancement Calcifications
Teratoma	Infant to young adult	Calcifications Macroscopic fat Fat-fluid level (sebum)
Renal/adrenal neoplasm with tumor thrombus	Known primary mass Symptoms of renal mass (ie, hematuria) Symptoms of functional adrenal mass	Presence of contiguous primary renal or adrenal mass
Hematoma	Trauma Anticoagulation therapy Blood dyscrasia	High-attenuation collection No enhancement Signs of trauma Intrinsic T1 hyperintense signal Low T2 signal intensity hemosiderin rim
Retroperitoneal fibrosis	Predisposing condition to retroperitoneal fibrosis History of immunoglobulin G4 (IgG4) disease	Characteristic location of fibrosis surrounding the abdominal aorta and proximal common iliac arteries centered at L4 Signs of volume loss, including an aorta that hugs the spine and medially deviated ureters Low T2 signal intensity Delayed enhancement pattern
Castleman disease	Young patient	Calcifications Intense early enhancement pattern Presence of satellite nodules Concomitant hepatosplenomegaly, ascites, and retroperitoneal fascial thickening

Figure 1. Extravascular retroperitoneal leiomyosarcoma in a 46-year-old woman with a 3-day history of right lower quadrant pain. **(a–c)** Axial **(a)**, sagittal **(b)**, and coronal **(c)** contrast-enhanced CT images show a heterogeneous enhancing retroperitoneal mass (*), posterior to the IVC (arrow in **a**) and separate from the kidney (arrow in **b**) and adrenal glands (black arrow in **c**). Note the invasion of the psoas muscle (white arrow in **c**). **(d–h)** Coronal T2-weighted single-shot fast spin-echo (SSFSE) **(d)**, axial T1-weighted fat-saturated **(e)**, axial contrast-enhanced T1-weighted fat-saturated **(f)**, axial diffusion-weighted **(g)**, and axial apparent diffusion coefficient (ADC) **(h)** MR images show a mass (* in **d**) with high T2 signal intensity and areas of hemorrhage (* in **e**), heterogeneous enhancement (arrow in **f**), and restricted diffusion (* in **g**, arrow in **h**). **(i)** Gross photograph of the mass shows areas of hemorrhage and necrosis (arrow). **(j)** Low-power photomicrograph shows spindle cells with mitoses and nuclear atypia (arrows) (hematoxylin-eosin [H-E] stain).

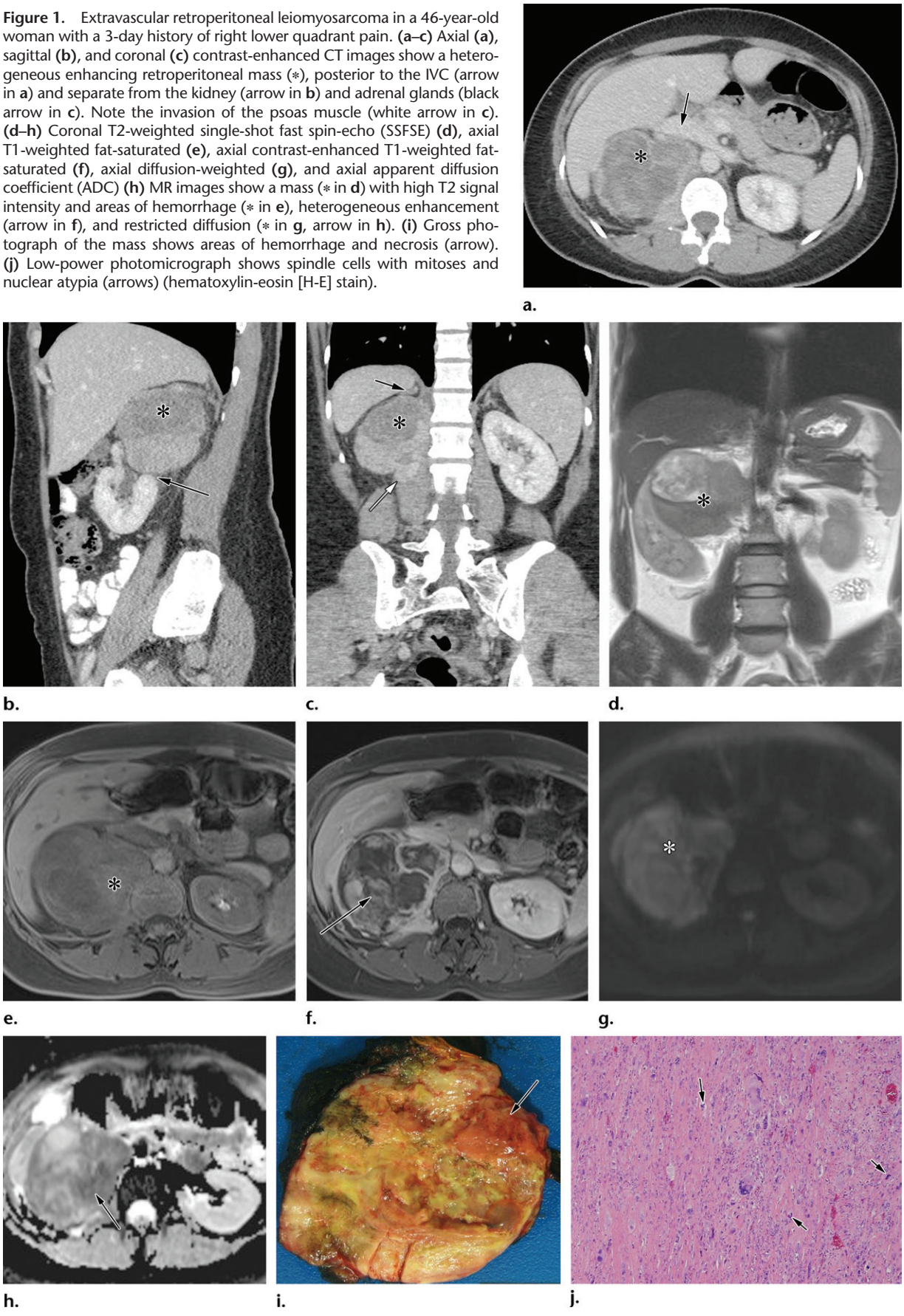
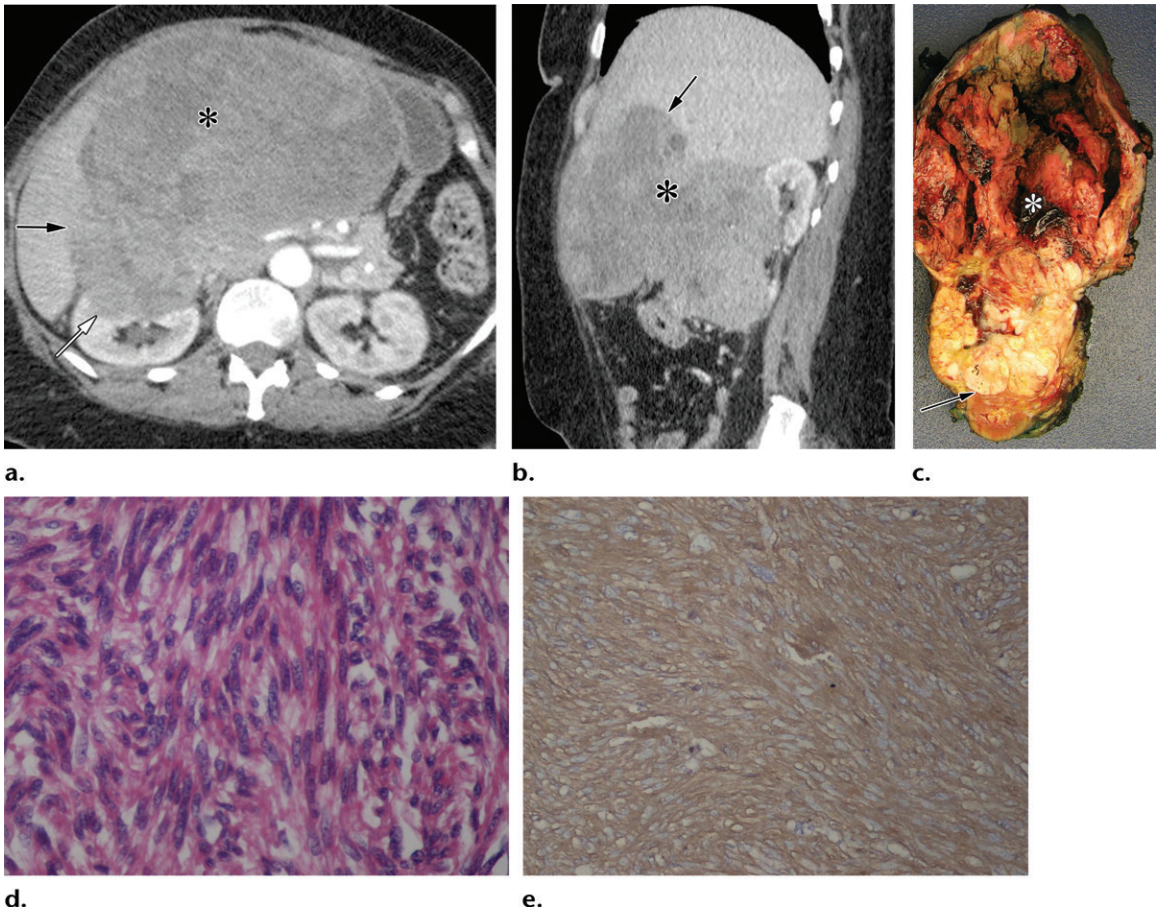


Figure 2. Extravascular retroperitoneal leiomyosarcoma in a 64-year-old woman with a 2-day history of abdominal pain and nausea. **(a, b)** Axial **(a)** and sagittal **(b)** contrast-enhanced CT images show a heterogeneous right-sided retroperitoneal mass (*). Note the invasion into the liver (black arrow) and kidney (white arrow in **a**). **(c)** Gross photograph of the mass shows invasion of the right kidney (arrow) and areas of hemorrhage and necrosis (*). **(d)** High-power photomicrograph shows the typical spindle cells seen in leiomyosarcoma (H-E stain). **(e)** Low-power photomicrograph shows diffuse positivity, compatible with a smooth muscle tumor such as retroperitoneal leiomyosarcoma (smooth muscle actin [SMA] stain).



be seen. In large masses, hyalinized hypocellular zones and coagulative tumor necrosis are common features. The tumor cell nuclei are typically centrally located, elongated, and blunt ended. Varying degrees of nuclear hyperchromasia and pleomorphism usually manifest. Mitotic figures and atypical mitoses are common (Fig 1). Cytoplasm varies from eosinophilic to pale (1).

Leiomyosarcomas may contain distinct regions with a nonspecific, poorly differentiated, and pleomorphic appearance compared with that of more typical areas, which can be considered dedifferentiated leiomyosarcoma. Rarely, leiomyosarcomas can contain osteosarcomatous or rhabdomyosarcomatous components (1).

Leiomyosarcomas can be graded using the Federation Nationale des Centres de Lutte Contre le Cancer (FNCLCC) or National Cancer Institute (NCI) systems. Both the FNCLCC and NCI systems are soft-tissue sarcoma classification systems rather than specific leiomyosarcoma grading systems.

The FNCLCC system uses scores for tumor differentiation, degree of necrosis, and mitotic count to determine the overall tumor grade. The NCI system uses histologic type and subtype, location, amount of tumor necrosis, degree of pleomorphism, and mitotic activity to determine tumor grade. Tumor grades range from 1 to 3 with both systems. The histologic subtypes of leiomyosarcoma used in these grading systems include well-differentiated leiomyosarcoma, conventional leiomyosarcoma, and poorly differentiated/pleomorphic/epithelioid leiomyosarcoma (13–15).

Immunophenotype

The most useful immunohistochemical stains are traditional smooth muscle markers, including SMA, desmin, and h-Caldesmon (11) (Fig 2). These markers are positive in more than 70% of cases. Since these markers are not entirely specific for smooth muscle, two positive markers are more supportive of the diagnosis of leiomyosarcoma

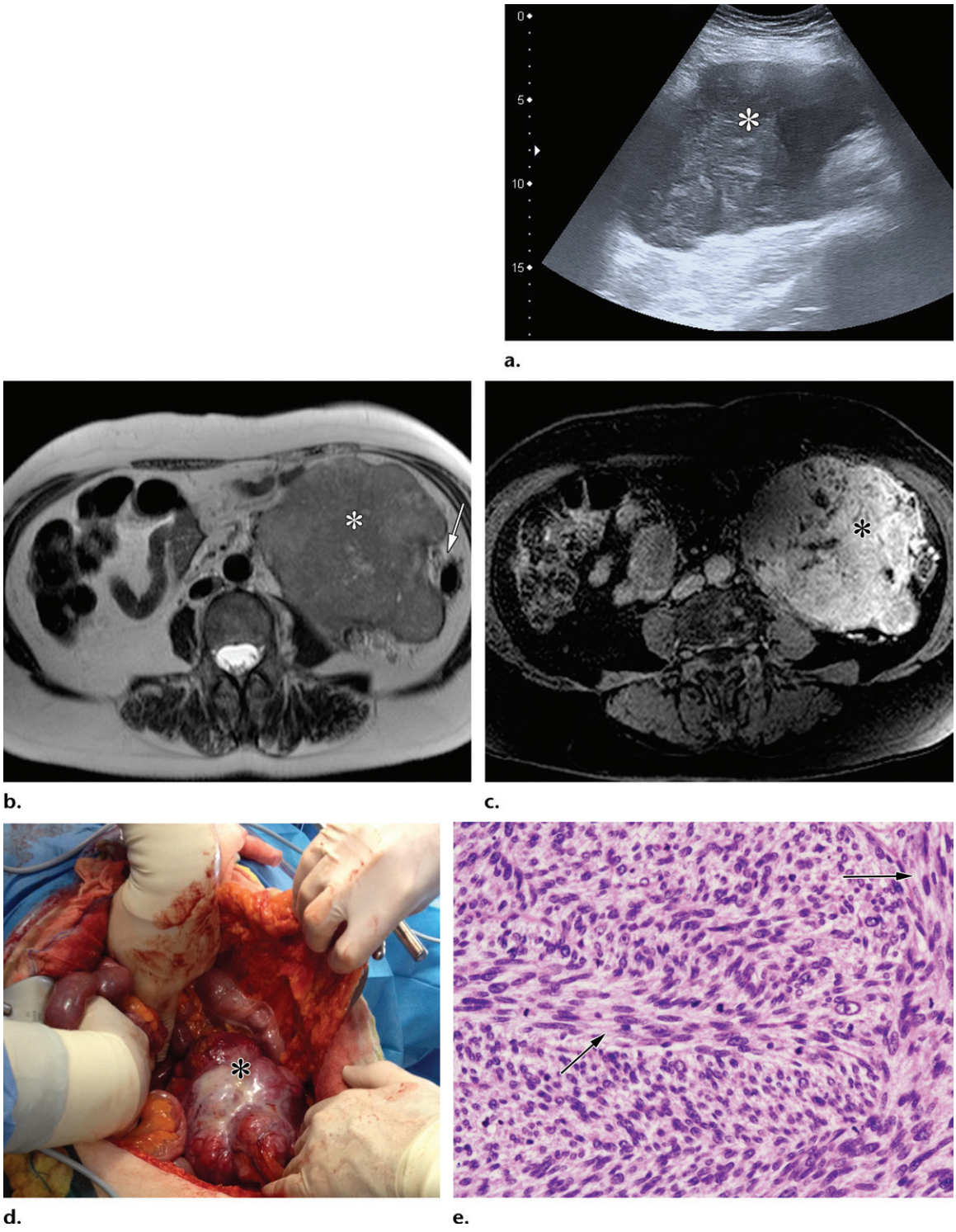
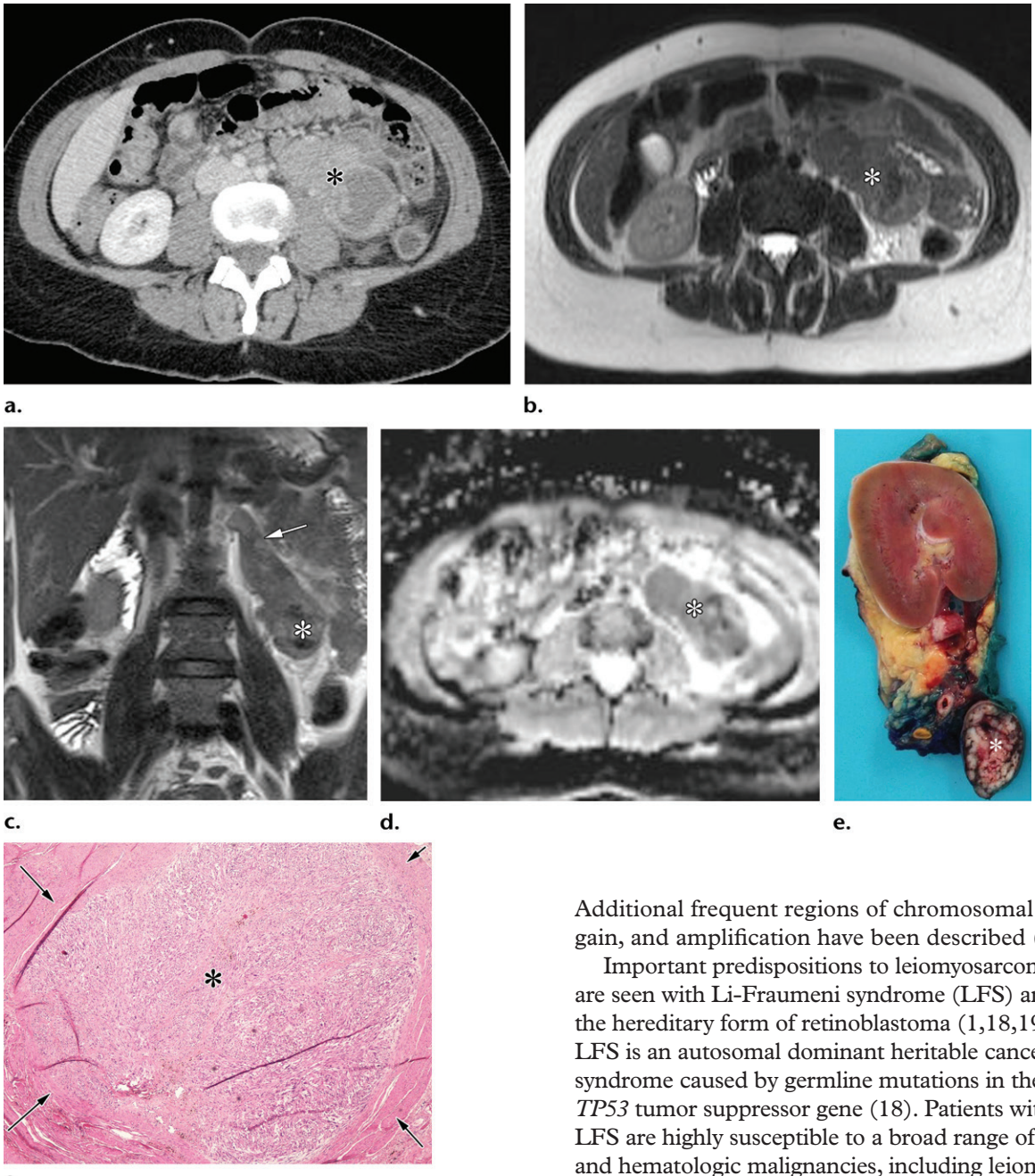


Figure 3. Extravascular retroperitoneal leiomyosarcoma in a 64-year-old woman with increasing vague abdominal pain. **(a)** Gray-scale US image shows a left-sided heterogeneous mass (*). **(b, c)** Axial T2-weighted SSFSE **(b)** and axial contrast-enhanced T1-weighted fat-saturated **(c)** MR images show a heterogeneous left-sided retroperitoneal mass, with high T2 signal intensity (* in **b**) and heterogeneous enhancement (* in **c**). Note the close approximation to the left colon (arrow in **b**). **(d)** Intraoperative photograph shows the retroperitoneal mass (*). **(e)** High-power photomicrograph shows a sharply marginated fascicle of spindle cells (arrows), typically seen in leiomyosarcoma (H-E stain).

than one positive marker. In tumors containing a dedifferentiated component, the smooth muscle markers will be negative in the dedifferentiated component. Additionally, focal positivity for keratin, epithelial membrane antigen, CD34, and S100 protein may be seen. CD117 (KIT), a marker for gastrointestinal stromal tumors, is negative (1).

Figure 4. Intra- and extravascular retroperitoneal leiomyosarcoma in a 49-year-old woman who presented to the emergency department with left lower quadrant pain. **(a)** Axial contrast-enhanced CT image shows a heterogeneous left-sided retroperitoneal mass (*). **(b–d)** Axial **(b)** and coronal **(c)** T2-weighted SSFSE MR images and axial ADC image **(d)** show a heterogeneous left-sided mass (* in **b** and **c**) with restricted diffusion (* in **d**). The mass appears to follow the course of the left ovarian vein on the coronal image (arrow in **c**). **(e)** Gross photograph shows the tumor in the left ovarian vein (*). **(f)** Low-power photomicrograph shows fascicles of spindle cells (*), representing the leiomyosarcoma, in the left ovarian vein (arrows) (H-E stain).



Genetics

The karyotypes seen with leiomyosarcoma are highly complex, with an increased propensity for genomic alterations (16). Leiomyosarcomas are frequently associated with defects in *TP53*. Another frequent site of involvement is the retinoblastoma-cyclin D pathway, with genomic loss at 13q14, centered on the *RB1* gene (17). Additional frequent regions of chromosomal loss, gain, and amplification have been described (16).

Important predispositions to leiomyosarcoma are seen with Li-Fraumeni syndrome (LFS) and the hereditary form of retinoblastoma (1,18,19). LFS is an autosomal dominant heritable cancer syndrome caused by germline mutations in the *TP53* tumor suppressor gene (18). Patients with LFS are highly susceptible to a broad range of solid and hematologic malignancies, including leiomyosarcoma. Even in sporadic leiomyosarcoma, *TP53* is mutated in 25% of cases, including biallelic *TP53* inactivation in up to one-half of cases.

Hereditary retinoblastoma, a rare eye cancer caused by a germline mutation in the *RB1* tumor suppressor gene, is associated with secondary tumors, including soft-tissue sarcoma. Leiomyosarcoma is the most common subtype of soft-tissue sarcoma seen in this patient population, with the majority diagnosed more than 30 years after retinoblastoma diagnosis (19).

Recent data suggest multiple molecular subtypes of leiomyosarcoma, with differing frequencies of specific genomic changes and varying prognoses. Expression of receptor tyrosine kinase–like orphan receptor 2 (ROR2) has been shown to play a role in the invasiveness of leiomyosarcoma in vitro and is predictive of a poor clinical outcome (1).

Management and Prognosis

Patients with retroperitoneal soft-tissue sarcomas, including leiomyosarcomas, are commonly managed at referral centers by multidisciplinary teams who have experience treating soft-tissue sarcomas (20). Imaging is an important part of the evaluation of any patient with suspected retroperitoneal leiomyosarcoma. The most commonly used imaging modalities include CT of the chest, abdomen, and pelvis and/or MRI of the abdomen and pelvis (21). In the setting of suspected retroperitoneal soft-tissue sarcoma, including leiomyosarcoma, preoperative image-guided core biopsy is indicated if the diagnosis is unclear after imaging or if a definitive histologic diagnosis is required to plan neoadjuvant or palliative therapy (8,22).

The American Joint Committee on Cancer's TNM staging system is the most common method of staging soft-tissue sarcoma, including retroperitoneal leiomyosarcoma. The staging is based on pathologic findings and includes tumor size, nodal status, metastases, and tumor grade based on the FNCLCC system.

The T stage is based on tumor size. Tumors that are less than 5 cm in greatest dimension are T1 disease. Tumors that are greater than 5 cm and less than 10 cm are T2 disease. Tumors that are greater than 10 cm and less than 15 cm are T3 disease. Tumors that are greater than 15 cm are T4 disease. Lymph node status is defined as N0 or N1. N1 disease includes regional lymph node metastases. Metastases are defined as present (M1) or absent (M0).

Stage I disease is divided into stage IA and stage IB. Stage IA tumors are limited to T1 tumors that are also grade 1. Stage IB tumors are T2–T4 tumors with no evidence of lymph node or distant metastases. Stage II tumors are grade 2 tumors that are less than 5 cm (T1). Stage III is divided into stage IIIA and stage IIIB. Stage IIIA tumors are T2 tumors that are also grade 2 or 3. Stage IIIB tumors are T3 or T4 tumors that are grade 2 or 3 or any T stage or grade with lymph node metastases (N1). Stage IV disease requires distant metastases (M1) (21).

If the patient's performance status allows, first-line treatment consists of surgical resection, with the goal of negative margins (20,23). Radical surgery is often needed, including the resection of involved organs. For tumors with vascular involvement or of vascular origin, surgery involves resection of the tumor with either vessel reconstruction or ligation. The precise role of radiation therapy and chemotherapy is not clear owing to the low numbers of patients affected by retroperitoneal leiomyosarcomas. The use of chemotherapy and radiation therapy has been described in both the neoadjuvant and adjuvant settings. When employed in the neoadjuvant setting, the goal of preoperative radiation therapy or chemotherapy is to reduce tumor bulk to facilitate resection with negative margins. Adjuvant chemotherapy and/or radiation therapy is used in some centers with the goal of reducing local and distant recurrence (6,8).

Retroperitoneal leiomyosarcomas are often fatal owing to local recurrence and distant metastases. Since they are typically large at diagnosis, leiomyosarcomas are often difficult or impossible to resect with clear margins. The adequacy of surgical resection is the most important predictor of prognosis (20,23). Histologic grade and the presence of osseous involvement are other reliable prognostic factors (1). The 5-year local recurrence–free survival after complete resection of soft-tissue sarcoma ranges between 55% and 78%. Local recurrence accounts for 75% of sarcoma-related deaths. The overall 5-year survival for retroperitoneal soft-tissue sarcoma is 39%–68%.

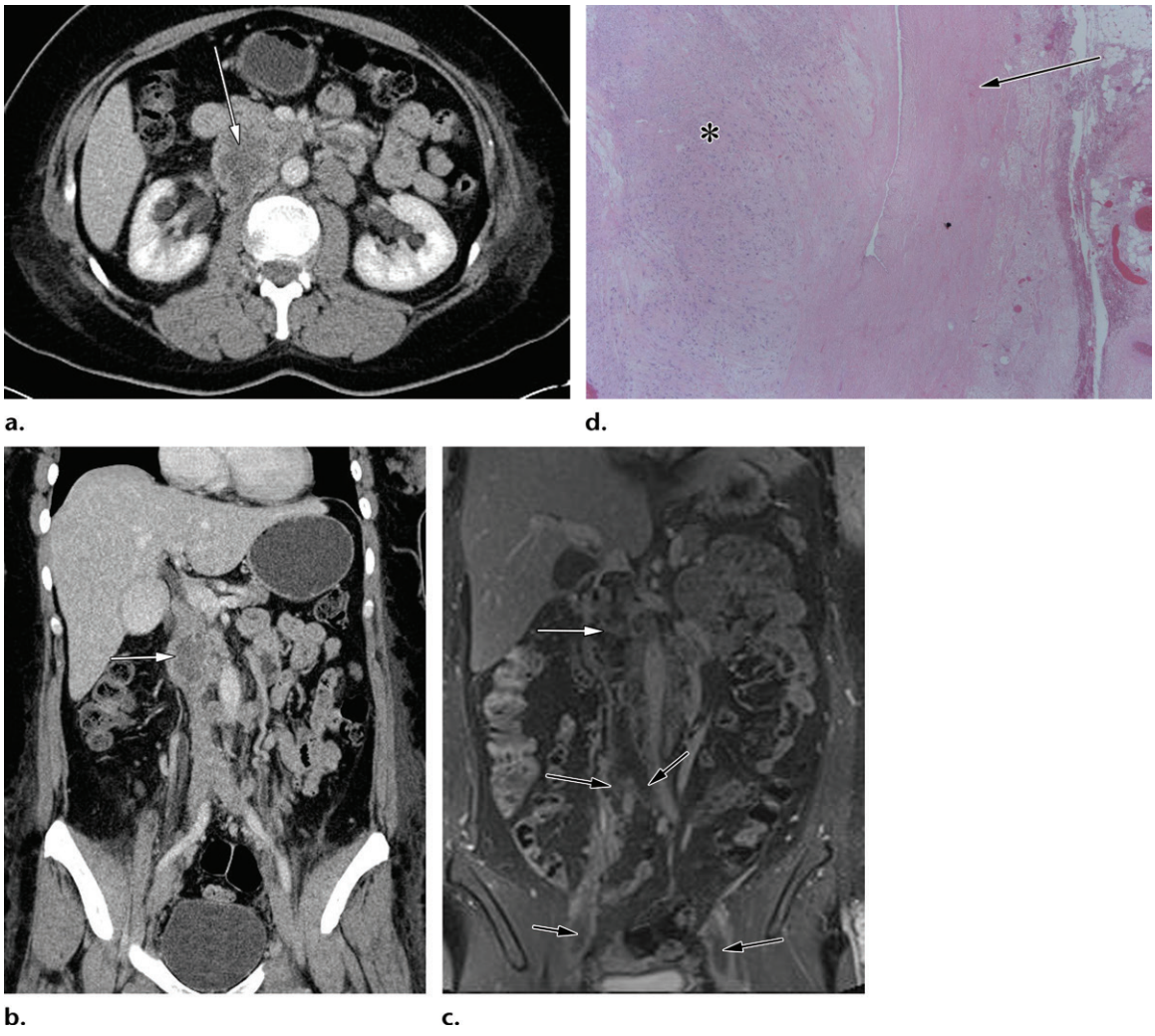
Imaging plays a critical role in the follow-up of patients with retroperitoneal leiomyosarcoma. In patients treated with surgical resection, National Comprehensive Cancer Network guidelines recommend a postoperative imaging strategy of performing CT or MRI of the abdomen and pelvis every 3–6 months for 2–3 years, then every 6 months for the next 2 years, then annually. Regular imaging of the chest, preferably with CT, is also recommended (21).

Imaging Features

Retroperitoneal leiomyosarcomas classically appear as large soft-tissue masses, often with areas of necrosis, hemorrhage, or cystic change (Fig 1). Calcifications are uncommon, except in rare cases of osteosarcomatous differentiation. The mean tumor size is approximately 11.3 cm for retroperitoneal leiomyosarcomas without vascular involvement. In cases with vascular involvement, mean tumor size is slightly smaller at 10.4 cm (7).

Retroperitoneal leiomyosarcomas are usually located in the perirenal or posterior pararenal spaces (7). They exhibit three major patterns of growth. The most common is an entirely extra-

Figure 5. Intravascular retroperitoneal leiomyosarcoma in a 46-year-old woman who presented with increasing bilateral lower extremity swelling over 18 months. **(a, b)** Axial **(a)** and coronal **(b)** contrast-enhanced CT images show an enhancing mass in the IVC (arrow). **(c)** Coronal T1-weighted fat-saturated MR image obtained after the administration of contrast material (postcontrast) shows the enhancing mass in the IVC (white arrow). Note the enhancing thrombus in the common iliac veins and external iliac veins (black arrows). **(d)** High-power photomicrograph shows the tumor (*) in the IVC (arrow) (H-E stain).

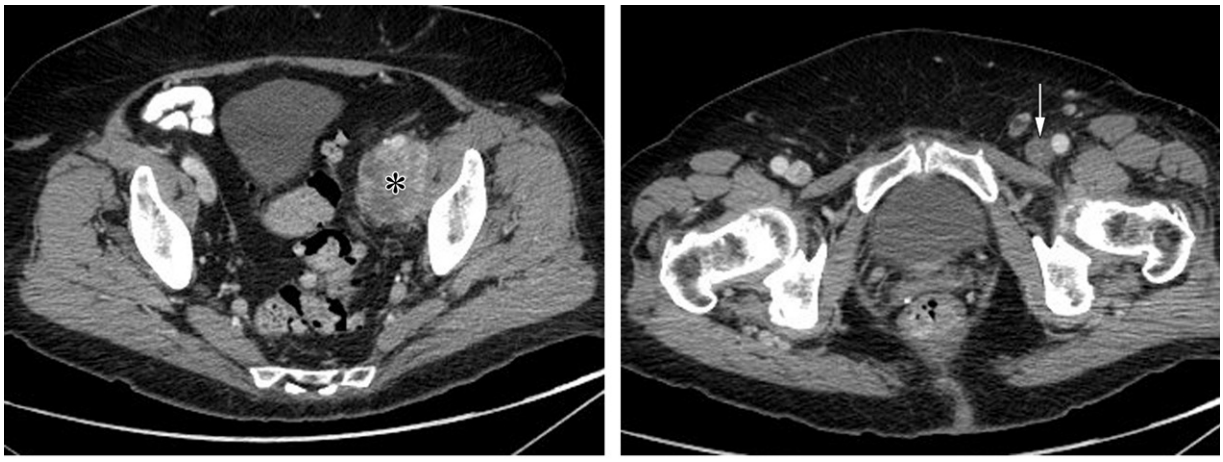


vascular or extraluminal pattern, accounting for 62% of cases (Figs 1–3). In one-third of cases, the pattern of growth includes both extravascular and intravascular components (Fig 4). The least common pattern of growth, occurring in only 5% of cases, is an entirely intravascular or intraluminal mass (10) (Fig 5).

Intravascular tumors can be localized to three segments of the IVC, with respect to the hepatic veins and renal veins. Segment 1 of the IVC is located caudal to the renal veins. Approximately 25%–37% of intravascular cases involve segment 1. Segment 2 is caudal to the hepatic veins but cranial to the renal veins. This is the most common site of disease, accounting for 43%–69% of intravascular cases. Segment 3 is located cranial to the hepatic veins. Segment 3 is the least commonly affected segment, representing 6%–20% of intravascular cases (7,9).

Radiologic imaging plays a key role in determining the possibility of surgical resection, given its ability to determine the mass's precise anatomic relationship to key retroperitoneal organs and major vascular structures. Imaging also helps detect metastases in a large number of cases, altering the patient's prognosis and treatment options. Specifically, in extravascular retroperitoneal leiomyosarcoma, metastases are seen at the time of diagnosis in approximately 9% of cases but develop in the large majority of cases during follow-up (7). The most common sites of metastases are the lungs (65%), peritoneum (53%), liver (53%), muscle (41%), bones (35%), and lymph nodes (35%) (7).

In leiomyosarcoma with intravascular involvement, metastases are seen at diagnosis in 23% of cases and are common at follow-up. Sites of metastatic involvement for tumors with intravascular



a. b.

Figure 6. Retroperitoneal leiomyosarcoma with bland thrombus in a 76-year-old woman who presented to the emergency department with left leg pain and swelling. **(a)** Axial contrast-enhanced CT image of the pelvis shows an enhancing mass along the left pelvic sidewall (*), in the region of the left external iliac vein, diagnosed as leiomyosarcoma. **(b)** Axial contrast-enhanced CT image obtained inferior to **a** shows a bland thrombus in the left common femoral vein (arrow).

involvement include the lungs (59%), liver (50%), peritoneum (41%), pleura (27%), muscle (23%), bones (14%), lymph nodes (14%), pancreas (9%), renal/perirenal space (5%), and adrenal glands (5%).

Ultrasonography

Retroperitoneal leiomyosarcomas appear as lobulated solid masses, often with irregular cystic spaces secondary to hemorrhage and necrosis (7) (Fig 3). The soft-tissue components are isoechoic to hyperechoic compared to the liver. The irregular cystic spaces may appear simple or contain low-level echoes. In tumors with an intravascular pattern of growth, the findings include an intraluminal solid mass with internal vascular flow at Doppler US. The tumors may appear homogeneous when small but become increasingly heterogeneous as they enlarge. The IVC is often expanded when intravascular tumors are large (10).

Computed Tomography

At CT, retroperitoneal leiomyosarcomas are depicted as large lobulated masses (10). The masses are predominantly solid but often contain cystic spaces or necrosis (Figs 1, 3). The solid components are hyperattenuating relative to muscle on postcontrast images in 56%–61% of cases. The enhancement pattern is heterogeneous in nearly all cases. Necrosis is identified as irregular hypoattenuating areas without enhancement in 28%–38% of cases. Calcifications are uncommonly seen (7,10). Collateral vessels are a common finding, seen in approximately 61% of cases (7). Local invasion, including involvement of the right kidney, liver, right adrenal gland, pancreas, stomach, and spine, is common (Fig 2). Hematogenous spread of metastases, especially to the lungs (59%–65%) and liver (50%–53%), is more common than lymphatic metastases (14%–35%) (7).

In intravascular leiomyosarcomas, the findings are consistent with tumor thrombus. The typical findings of tumor thrombus include dilatation of the vessel with heterogeneous enhancement of the intraluminal lesion. The mass may result in near-complete obstruction of the vascular lumen, often the IVC or renal vein (10) (Fig 5). Care should be taken to differentiate the enhancing tumor from bland thrombus, which can also be found in the vessel (Fig 6). The use of pre- and postcontrast CT is helpful in confirming enhancement of the tumor thrombus.

Magnetic Resonance Imaging

Retroperitoneal leiomyosarcomas demonstrate hypointense to isointense T1 signal intensity and high T2 signal intensity in the solid components of the tumor (7,9) (Figs 1, 3). Areas of necrosis are typically T1 hypointense and T2 hyperintense compared with muscle (10). If hemorrhagic necrosis manifests, the T1 signal may be hyperintense relative to that of muscle. The solid portion of the tumor most commonly demonstrates heterogeneous enhancement (7).

In cases with intravascular tumor, black blood imaging sequences nicely show the degree of intravascular tumor extension by highlighting the hyperintense tumor compared with the hypointense luminal blood (10). Multiplanar postcontrast imaging is also useful to evaluate the extent of vascular involvement and to differentiate tumor from bland thrombus.

Differential Diagnosis: Neoplasms

Adenopathy

Lymphoma.—Both Hodgkin and non-Hodgkin lymphoma can involve the retroperitoneum. Lymphoma in the retroperitoneum may manifest with multiple enlarged lymph nodes or a masslike conglomeration of lymph nodes, the latter more strongly resembling leiomyosarcoma (24). When masslike, lymphoma is most often well defined and homogeneous and shows mild contrast enhancement (25). Lymphoma commonly displaces structures, including anteriorly displacing the aorta from the spine, but typically does not invade the major vascular structures (26). When imaging patients with non-Hodgkin lymphoma involving the abdominal lymph nodes, it is not uncommon to encounter sites of extranodal lymphoma, especially in the gastrointestinal tract (25). Calcifications and necrosis are uncommon in the absence of treatment.

At MRI, lymphoma is most commonly T1 hypointense and T2 iso- or hyperintense, with moderate enhancement. Although the MRI enhancement pattern typically seen with lymphoma is homogeneous, up to one-fourth of cases can demonstrate heterogeneous enhancement (4). Imaging features that can help distinguish lymphoma from leiomyosarcoma include findings of extranodal lymphoma, multiple sites of adenopathy, absence of vascular involvement, and lack of necrosis. Although nonspecific, in selected cases clinical features may suggest the diagnosis of lymphoma over leiomyosarcoma. Clinical features to consider include the presence of B symptoms (fever, night sweats, and weight loss) and an elevated level of LDH (27).

Retroperitoneal Lymph Node Metastases.—The retroperitoneal lymph nodes are a common site of metastatic spread from a variety of primary malignancies. Primary neoplasms that commonly spread to retroperitoneal lymph nodes include testicular carcinoma, prostate adenocarcinoma, renal cell carcinoma, and cervical carcinoma, among many others (28–30). Retroperitoneal metastatic disease may appear as one or more discrete enlarged lymph nodes or as a conglomerate mass (30). When retroperitoneal adenopathy appears as a conglomerate mass, it may mimic retroperitoneal leiomyosarcoma. Important imaging features that may be common to leiomyosarcoma and metastases include large size, predominantly solid appearance, irregular areas of necrosis, and heterogeneous enhancement pattern (10,30). Clinical and imaging features may help suggest metastases over retroperitoneal leiomyosarcoma. Clinically, if a patient has a history of a primary malignancy with a propensity to spread to the retroperitoneum, metastatic disease should be the primary consideration.

Elevated levels of tumors markers, such as prostate-specific antigen in prostate cancer or β–human chorionic gonadotropin (β-hCG) and α-fetoprotein (AFP) in testicular cancer, may help suggest metastases. Also, metastases have a much higher prevalence than leiomyosarcoma or any primary retroperitoneal malignancy and therefore should be high on the differential diagnosis for any retroperitoneal mass. Imaging, such as with scrotal US, may help by detecting a primary lesion with malignant features or additional areas of metastatic spread, particularly lymph node metastases, an uncommon finding in leiomyosarcoma.

Soft-Tissue Sarcomas

The soft-tissue sarcomas, including leiomyosarcoma, are mesodermal-origin tumors. They can be broadly categorized as tumors of adipose tissue, connective tissue, vascular tissue, skeletal muscle, and smooth muscle. A detailed discussion of the spectrum of soft-tissue sarcomas is beyond the scope of this article. Instead, we review important features of retroperitoneal liposarcoma, as it is the one the reader will most likely encounter in daily practice.

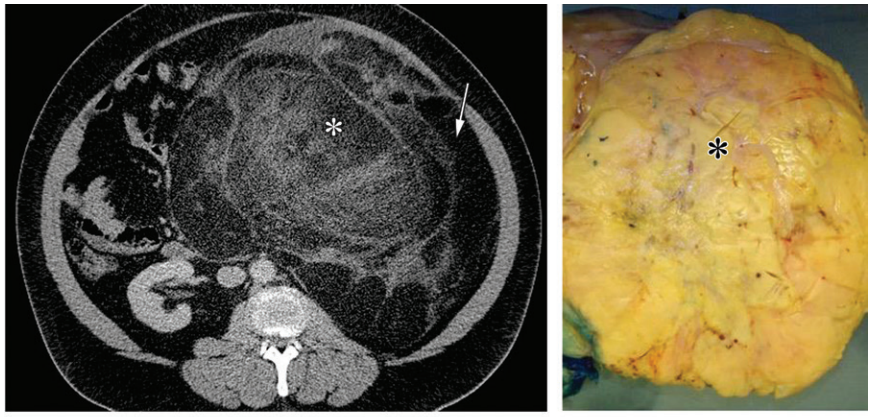
Liposarcoma.—Liposarcoma (Fig 7) is the most common primary retroperitoneal sarcoma. It most often affects patients 50–70 years of age, a similar age group as patients with leiomyosarcoma. Liposarcomas are usually large at presentation, similar to leiomyosarcoma. The tumor composition varies on the basis of the histologic subtype.

Well-differentiated tumors appear as well-defined lesions with internal macroscopic fat and minimal internal soft tissue, commonly in the form of thin septa (31). Well-differentiated tumors are easily distinguished from leiomyosarcoma, given their internal macroscopic fat. High-grade liposarcomas, including pleomorphic liposarcoma, round cell liposarcoma, and extensively dedifferentiated liposarcoma, may contain little or no macroscopic fat. In cases without macroscopic fat, differentiating liposarcoma from leiomyosarcoma is more challenging. Calcification has been described in 30% of liposarcomas, an uncommon finding in leiomyosarcoma (4).

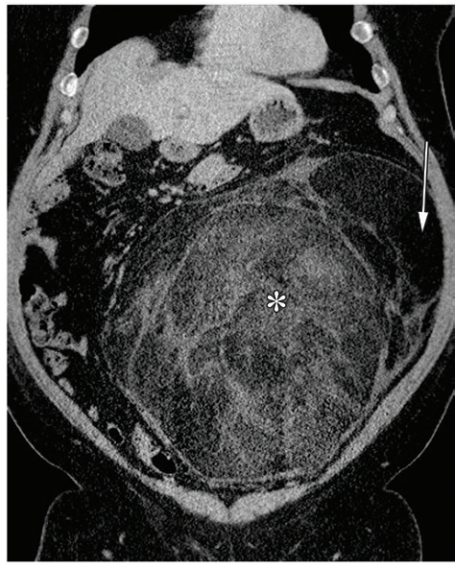
Neurogenic Tumors

Neurogenic tumors (Fig 8) account for 10%–20% of retroperitoneal neoplasms. Compared with

Figure 7. Well-differentiated retroperitoneal liposarcoma in a 44-year-old man who presented with vague abdominal pain. **(a, b)** Axial **(a)** and coronal **(b)** contrast-enhanced CT images show a heterogeneous mass (*) with macroscopic fat (arrow). **(c)** Gross photograph of the mass shows the typical canary yellow macroscopic fat (*).



a. c.



b.

retroperitoneal leiomyosarcomas, neurogenic tumors affect a younger patient population and have a better prognosis. The broad classification of neurogenic tumors includes the nerve sheath tumors (neurofibroma, schwannoma, and malignant nerve sheath tumor), tumors of the sympathetic ganglia (ganglioneuroma, ganglioneuroblastoma, and neuroblastoma), and paragangliomas (4,32).

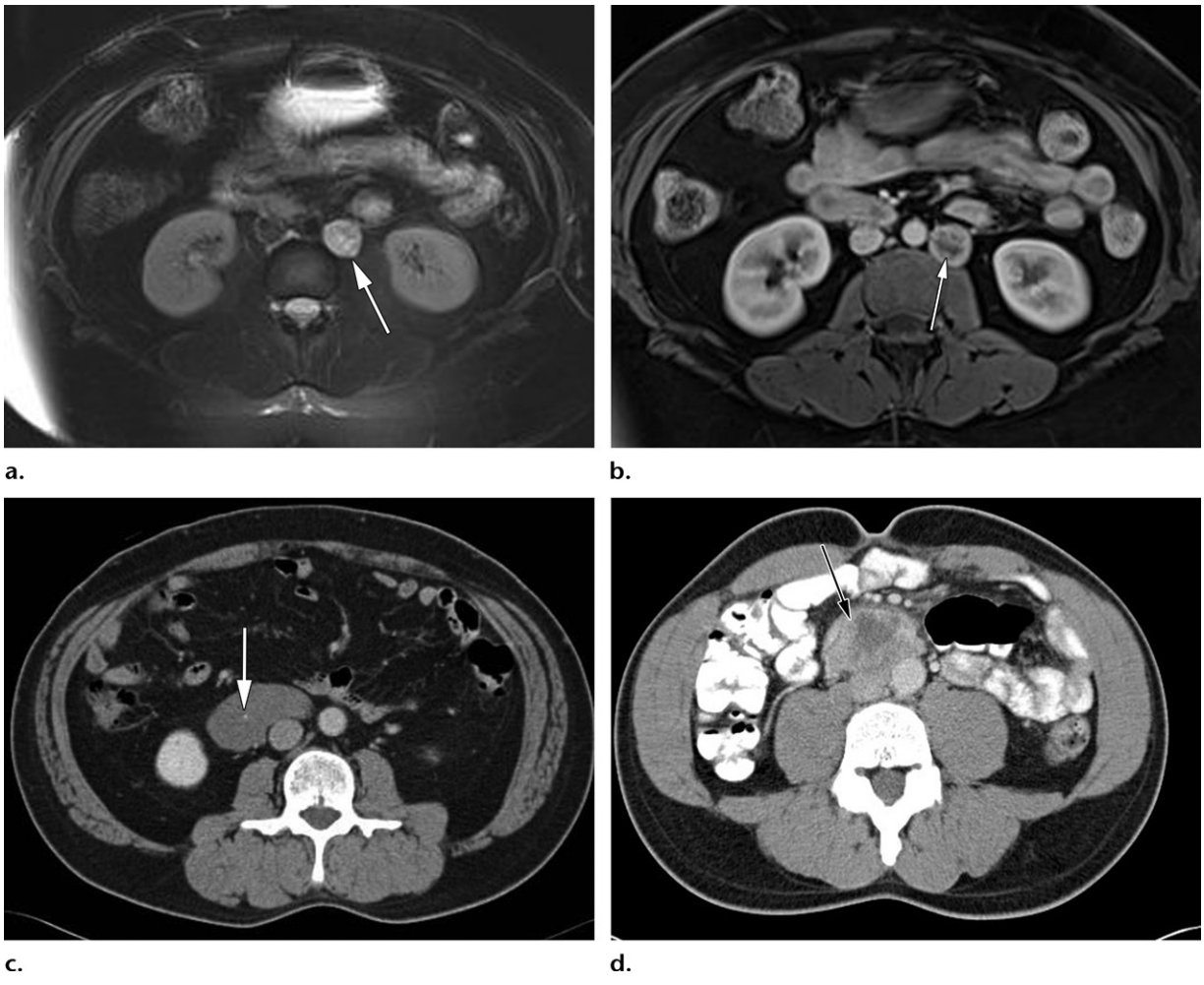
Neurofibroma.—Neurofibromas are benign tumors that can occur sporadically or in association with neurofibromatosis (32,33). They are more common in men than women and affect young patients, often 20–40 years of age (32). At CT, neurofibromas are usually homogeneously hypoattenuating and demonstrate uniform enhancement. At MRI, neurofibromas are typically T1 hypointense and T2 hyperintense and may have a target appearance, with low T2 signal intensity centrally and high T2 signal intensity peripherally (32). If the tumor arises in the neural foramen, it may have a characteristic dumbbell shape.

Occasionally these tumors develop myxoid degeneration, leading to a more heterogeneous appearance, similar to leiomyosarcoma. Plexiform neurofibromas, congenital lesions seen in patients with neurofibromatosis type 1, often appear as large infiltrative masses (33). Neurofibromas can often be distinguished from leiomyosarcomas on the basis of clinical features such as young patient age or known diagnosis of neurofibromatosis. Distinguishing imaging features include a homogeneous hypoattenuating appearance with uniform enhancement, dumbbell shape, or a target sign.

Schwannoma.—Schwannomas (Fig 8a, 8b) are benign tumors that account for 6% of retroperitoneal neoplasms (32). Schwannomas are usually an asymptomatic incidental finding at imaging. Schwannomas are more common in women than in men and occur in young to middle-aged patients, typically 20–50 years of age (32).

Schwannomas are often paraspinal or presacral in location. When small, schwannomas may appear round and homogeneous at CT and MRI. As these tumors enlarge, they become more heterogeneous, with areas of cystic change (4). Schwannomas may contain calcifications that have been described as punctate, mottled, or curvilinear. Clinical and imaging features including young patient age, paraspinal location, calcification, and absence of vascular involvement may help distinguish a schwannoma from a leiomyosarcoma. As schwannomas enlarge and become more heterogeneous, differentiation from leiomyosarcoma becomes more difficult.

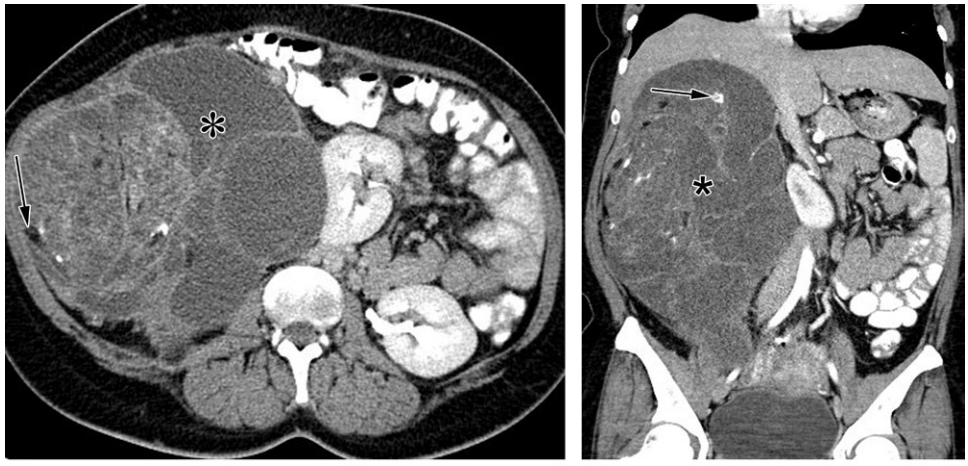
Figure 8. Neurogenic tumors. **(a, b)** Schwannoma in a 46-year-old woman who presented to the emergency department with abdominal pain. Axial T2-weighted fat-saturated **(a)** and contrast-enhanced T1-weighted fat-saturated **(b)** MR images show a left para-aortic retroperitoneal mass (arrow), with high T2 signal intensity in **a** and enhancement in **b**. **(c)** Ganglioneuroma in a 52-year-old man who presented with vague abdominal pain. Axial contrast-enhanced CT image shows a homogeneously enhancing retroperitoneal mass with calcification (arrow). The lack of necrosis and the presence of calcification suggest ganglioneuroma over leiomyosarcoma. **(d)** Paraganglioma in a 56-year-old man with uncontrolled hypertension. Axial contrast-enhanced CT image shows an enhancing retroperitoneal mass (arrow) anterior to the aorta and IVC, in the region of the organ of Zuckerkandl.



Ganglioneuroma.—Ganglioneuromas (Fig 8c) are benign tumors of the sympathetic ganglia that typically occur in children or adults 20–40 years of age. Up to 52% of these benign lesions occur in the retroperitoneum, either in the paravertebral region or in the adrenal medulla (4). At imaging, ganglioneuromas are well-circumscribed lobulated masses. At US, ganglioneuromas are homogeneously hypoechoic masses (34). They are hypoattenuating at CT with variable but typically weak homogeneous or heterogeneous enhancement.

Calcifications manifest in up to 60% of cases (34). At MRI, they are T1 hypointense, with variable T2 hyperintensity and enhancement, which often increases with time (34). They may demonstrate a whorled appearance at MRI (4). Necrosis and hemorrhage are uncommon features. Both clinical and imaging features are helpful in distinguishing ganglioneuroma from leiomyosarcoma. Clinically, ganglioneuromas occur in a younger patient population than leiomyosarcomas. The presence of calcifications and absence of necrosis in a paravertebral mass suggest ganglioneuroma over leiomyosarcoma (4).

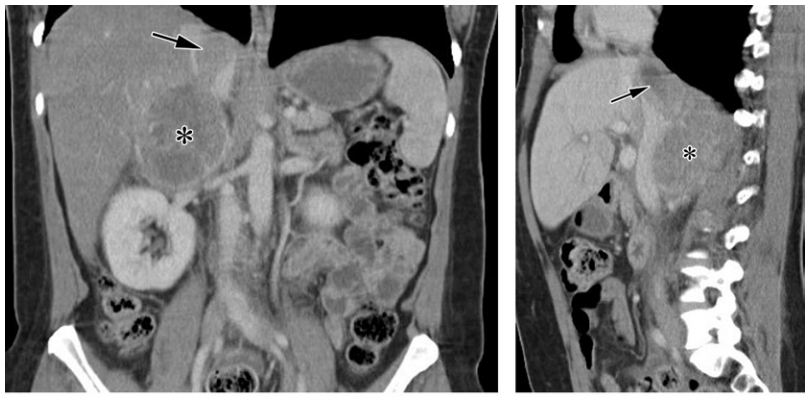
Paraganglioma.—Paragangliomas (Fig 8d) are tumors of the chromaffin cells that may occur at or separate from the adrenal medulla (35). Paragangliomas of the adrenal gland are referred to as pheochromocytomas. Paragangliomas are associated with a number of clinical syndromes including neurofibromatosis type 1, multiple endocrine neoplasia syndromes 2A and 2B, von Hippel–Lindau syndrome (VHL), and the Carney triad (35,36). Approximately 40% of paragangliomas are caused by germline mutations in one of 13



a. b.

Figure 9. Retroperitoneal teratoma in a 29-year-old woman with increasing abdominal pain and nausea for 3 months. Axial **(a)** and coronal **(b)** contrast-enhanced CT images demonstrate a heterogeneous mass (*) that contains both macroscopic fat (arrow in **a**) and calcification (arrow in **b**), typical for retroperitoneal teratoma.

Figure 10. Adrenal cortical neoplasm in a 44-year-old woman who presented with a 2-week history of epigastric abdominal pain radiating to her right flank and back with increasing shortness of breath. Coronal **(a)** and sagittal **(b)** contrast-enhanced CT images show an enhancing suprarenal retroperitoneal mass (*) with extension into the IVC (arrow), diagnosed as adrenal cortical neoplasm.



a. b.

predisposing genes, including the *RET* proto-oncogene and the *NF1*, *VHL*, and SDH genes (36).

Paragangliomas typically affect patients 20–40 years of age. Abdominal paragangliomas can manifest with symptoms of catecholamine excess (32). Extra-adrenal abdominal paragangliomas also frequently metastasize, seen in up to 42% of cases (32). Although they can occur throughout the retroperitoneum, extra-adrenal abdominal paragangliomas are most common at the organs of Zuckerkandl, near the inferior mesenteric artery origin (35).

Paragangliomas are usually large lobulated intensely enhancing soft-tissue masses, commonly with regions of necrosis and hemorrhage (32). Calcifications occur in 15% of cases (37). At MRI, paragangliomas are T1 hypointense, except for regions of internal hemorrhage. They are most commonly heterogeneous on T2-weighted images, with the small minority of cases being intensely T2 hyperintense. Fluid-hemorrhage levels can be seen.

Clinical features that help differentiate paraganglioma from leiomyosarcoma include younger patient population than leiomyosarcoma, clinical or laboratory evidence of catecholamine excess, and known diagnosis of a predisposing clinical syndrome or genetic abnormality. Imaging features that may suggest paraganglioma include location at the organ of Zuckerkandl, avid enhancement, and calcifications. Some features, including size, morphology, and necrosis, can mimic leiomyosarcoma (4).

Germ Cell Tumors

When germ cell tumors are encountered in the retroperitoneum, it is typically owing to metastatic adenopathy. Uncommonly, primary germ cell tumors can occur in the retroperitoneum. It is estimated that 3%–6% of extragonadal primary germ cell tumors occur in the retroperitoneum (38). Primary retroperitoneal germ cell tumors arise from pluripotent germ cells that

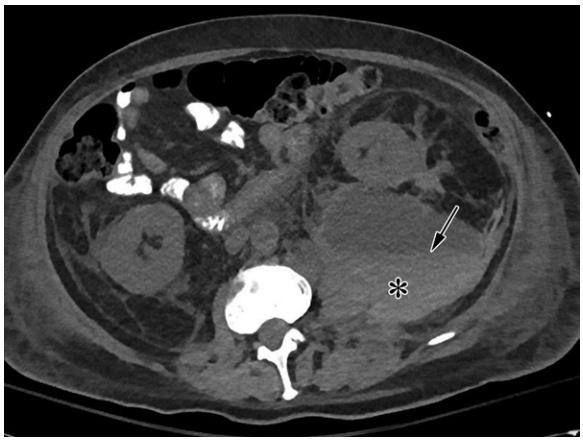


Figure 11. Retroperitoneal hematoma in a 45-year-old man with a history of trauma. Axial nonenhanced CT image shows a left retroperitoneal lesion with high-attenuation blood (*) and a fluid-fluid level (arrow), typical for retroperitoneal hematoma.

incompletely migrated to the genital ridges during embryologic development. The most common primary retroperitoneal germ cell tumor is teratoma (39).

Teratoma.—Teratomas (Fig 9) are tumors that contain components derived from at least two primitive germ cell layers. Pathologists describe teratomas as mature or immature on the basis of the degree of histologic differentiation (39). Immature teratomas are more likely to exhibit malignant behavior than mature teratomas (39). Teratomas occur in infants and young adults with a female predominance. The imaging appearance of a teratoma can be highly variable, but important suggestive imaging findings include calcification (may be toothlike), fat, and cystic components (4). A fat-fluid level related to sebum is pathognomonic. Teratomas can be differentiated from leiomyosarcoma by the distinct patient population and the presence of calcification and fat at imaging (4). In selected cases, elevated tumor marker levels such as AFP, β-hCG, or LDH may suggest germ cell origin of the retroperitoneal mass (38).

Retroperitoneal Organ–based Tumors

Large neoplasms arising from the retroperitoneal organs may mimic retroperitoneal leiomyosarcoma. This is especially true when the primary mass invades the IVC, mimicking the second most common pattern of growth for leiomyosarcoma. The most common primary malignancies to involve the retroperitoneal IVC in adult patients are renal cell carcinoma and adrenal cortical carcinoma. IVC involvement occurs in 4%–10% of renal cell carcinomas. IVC tumor thrombus can be seen in up to 30% of large right-sided adrenal cortical carcinomas (40) (Fig 10).

The key to distinguishing a primary renal or adrenal mass with secondary tumor thrombus from intravascular leiomyosarcoma is the presence of a contiguous primary malignancy. A variety of findings have been described in the literature to help differentiate primary retroperitoneal abnormalities from organ-based retroperitoneal neoplasms. These findings include the claw or beak sign, phantom organ sign, embedded organ sign, and prominent feeding artery sign (31). Occasionally, retroperitoneal leiomyosarcomas that are large and locally invasive of the kidney, adrenal gland, or bowel can be indistinguishable from a primary malignancy (Fig 2) (40).

Differential Diagnosis: Nonneoplastic Conditions

Fluid Collections

A variety of fluid collections can occur in the retroperitoneum, some of which may appear complex and mimic a soft-tissue mass. Examples of important retroperitoneal fluid collections include hematoma, abscess, phlegmon, urinoma, lymphocele, pseudocyst, and walled-off necrosis.

Hematoma.—The retroperitoneum is a common site of hematoma formation (Fig 11). Common causes of retroperitoneal hematoma include trauma, anticoagulation therapy, abdominal aortic aneurysm rupture, and a variety of blood dyscrasias (41). The imaging appearance of retroperitoneal hematoma varies with time. Acute and subacute hematomas are often higher in attenuation than simple fluid and may contain fluid-fluid levels (41). The imaging appearance of an acute or subacute hematoma could overlap with a heterogeneous retroperitoneal soft-tissue mass, the common imaging appearance of retroperitoneal leiomyosarcoma. This challenge of differentiation would be most often encountered at CT when only nonenhanced or postcontrast imaging was performed.

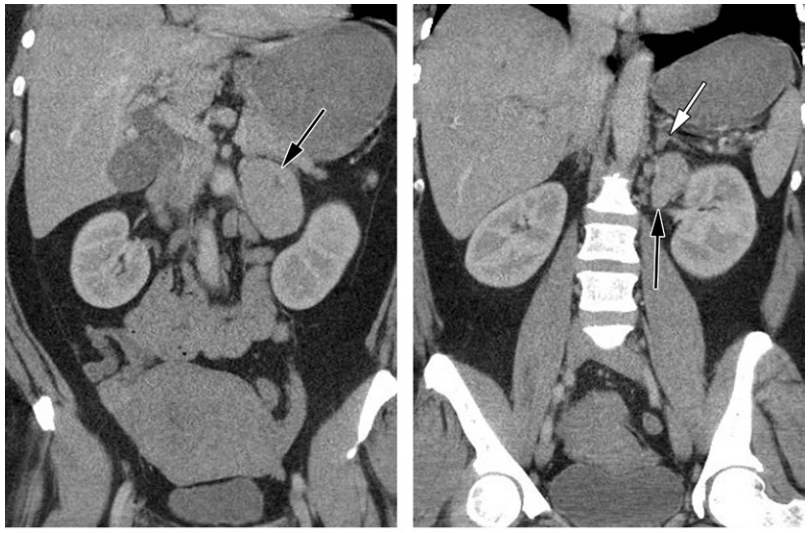


Figure 12. Castleman disease (hyaline vascular subtype) in a 44-year-old woman who presented with epigastric pain. Coronal contrast-enhanced CT images demonstrate a homogeneously enhancing left retroperitoneal mass (black arrows). Results of a biopsy confirmed Castleman disease, hyaline vascular subtype. Note that the mass is separate from the kidney and adrenal gland (white arrow in **b**).

a. **b.**

When both pre- and postcontrast CT images are available, the lack of enhancement should help differentiate hematoma from a soft-tissue mass.

At MRI, T1 hyperintense signal that does not suppress with fat saturation and the absence of enhancement would suggest hematoma. A subacute hematoma may show a thin peripheral rim with low signal intensity with all pulse sequences, corresponding to hemosiderin and inner high T1 signal intensity caused by methemoglobin (42). Often clinical factors, such as recent trauma, can help differentiate hematoma from retroperitoneal leiomyosarcoma.

Retroperitoneal Fibrosis

Retroperitoneal fibrosis is an uncommon condition of the retroperitoneal connective tissues that results in inflammatory and fibrotic changes in the retroperitoneal fat (43). Retroperitoneal fibrosis most often affects middle-aged patients. Retroperitoneal fibrosis was traditionally thought to be idiopathic in about two-thirds of cases. Currently, it is thought that about 50% of cases of idiopathic retroperitoneal fibrosis may be a symptom of IgG4–related disease (44). Retroperitoneal fibrosis may also be secondary to a variety of conditions, including the use of certain medications, infections, malignancy, prior surgery or radiation therapy, and Erdheim-Chester disease (44,45).

The clinical presentation of retroperitoneal fibrosis includes abdominal or flank pain and constitutional symptoms. Levels of serologic markers, including IgG4, erythrocyte sedimentation rate, and/or C-reactive protein, may be elevated (43). Imaging findings of retroperitoneal fibrosis include soft tissue surrounding the abdominal aorta and proximal common iliac arteries centered at L4. Given the fibrotic nature of the condition, the abdominal aorta is typically not displaced from the spine, and the ureters may be medially deviated.

At MRI, retroperitoneal fibrosis can be divided into two stages: acute inflammatory and fibrotic. In the inflammatory stage, the retroperitoneal soft tissue will enhance with administration of gadolinium contrast material, mimicking a neoplasm. In the later stage of disease, the fibrotic tissue will demonstrate decreased T2 signal intensity and show only mild delayed enhancement, findings characteristic of fibrotic tissue (45). Clinical factors, such as a known diagnosis of a predisposing condition to secondary retroperitoneal fibrosis, or other manifestations of IgG4-related disease, such as thyroiditis, mediastinitis, or sclerosing cholangitis, may help differentiation from a retroperitoneal neoplasm.

When CT or MRI show a characteristic location of the retroperitoneal abnormality, in addition to signs of volume loss, retroperitoneal fibrosis can be suggested over leiomyosarcoma. MRI findings of the late fibrotic phase of retroperitoneal fibrosis are specific and should be easily separated from leiomyosarcoma.

Castleman Disease

Castleman disease (Fig 12) is an uncommon condition characterized by lymphocyte proliferation (46). Castleman disease involves the abdomen and pelvis, including the retroperitoneum, in about 12% of cases (46). Castleman disease can be divided into four histopathogenetic subtypes or two broad clinical types. The four histopathogenetic subtypes are hyaline vascular, plasma cell, human herpesvirus–associated, and multicentric Castleman disease, not otherwise

specified (47). The two clinical categories of Castleman disease are localized or diffuse-type disease. Localized disease is primarily of the hyaline vascular subtype and has a good prognosis after adequate surgical resection. The diffuse type is more commonly of the plasma cell subtype and has a worse prognosis, often requiring systemic therapy (43).

Localized Castleman disease can manifest as a large solitary mass of soft-tissue attenuation or a dominant mass with satellite nodules. The masses are typically well defined and large, ranging from 3.5 to 8.0 cm in one study (46). Internal punctate calcifications and regions of cystic change or necrosis have been described (46). At MRI, the masses demonstrate hypointense to isointense T1 signal and hyperintense T2 signal. Enhancement is usually robust, occurring in the arterial phase and persisting on delayed phase images.

Diffuse-type Castleman disease manifests as multiple enlarged lymph nodes, typically with well-defined margins, homogeneous attenuation or signal intensity, and mild to moderate enhancement (46). Hepatosplenomegaly, ascites, and retroperitoneal fascial thickening may also be seen with diffuse disease (48). The localized type of Castleman disease can mimic leiomyosarcoma when it occurs in the retroperitoneum.

The most helpful clinical factor for differentiating Castleman disease from leiomyosarcoma is age. Localized Castleman disease most commonly affects adults in the 3rd or 4th decade of life, a younger population than typically affected by retroperitoneal leiomyosarcoma (47). Unfortunately, imaging features of a large soft-tissue mass with areas of necrosis may be common to both diagnoses. The most helpful imaging feature for differentiating Castleman disease from retroperitoneal leiomyosarcoma is the characteristic early intense enhancement pattern.

Conclusion

Retroperitoneal leiomyosarcoma is an important malignant neoplasm with absent or nonspecific clinical symptoms. Pathologic features are a spindle cell neoplasm, with centrally located elongated nuclei and varying degrees of nuclear hyperchromasia, pleomorphism, and mitotic figures. Imaging findings can be variable but most commonly include a large, predominantly extravascular soft-tissue mass with necrosis. Radiologists play a number of key roles in the care of patients with leiomyosarcoma, including suggesting the diagnosis at imaging, performing percutaneous core biopsy, assisting with treatment planning, and measuring response to therapy at follow-up. Familiarity with retroperitoneal leiomyosarcoma and its appropriate differential diagnosis will help the radiologist consider this diagnosis when encountering a retroperitoneal mass.

References

1. Fletcher CDM, Bridge JA, Hogendoorn PCW, Mertens F. WHO classification of tumours of soft tissue and bone. Lyon, France: IARC, 2013.
2. Wile AG, Evans HL, Romsdahl MM. Leiomyosarcoma of soft tissue: a clinicopathologic study. Cancer 1981;48(4):1022–1032.
3. Adam YG, Oland J, Halevy A, Reif R. Primary retroperitoneal soft-tissue sarcomas. J Surg Oncol 1984;25(1):8–11.
4. Rajiah P, Sinha R, Cuevas C, Dubinsky TJ, Bush WH Jr, Kolokythas O. Imaging of uncommon retroperitoneal masses. RadioGraphics 2011;31(4):949–976.
5. de Saint Aubain Somerhausen N, Fletcher CD. Leiomyosarcoma of soft tissue in children: clinicopathologic analysis of 20 cases. Am J Surg Pathol 1999;23(7):755–763.
6. Mullinax JE, Zager JS, Gonzalez RJ. Current diagnosis and management of retroperitoneal sarcoma. Cancer Contr 2011; 18(3):177–187.
7. Cooley CL, Jagannathan JP, Kurra V, et al. Imaging features and metastatic pattern of non-IVC retroperitoneal leiomyosarcomas: are they different from IVC leiomyosarcomas? J Comput Assist Tomogr 2014;38(5):687–692.
8. Olimpiadi Y, Song S, Hu JS, et al. Contemporary management of retroperitoneal soft tissue sarcomas. Curr Oncol Rep 2015;17(8):39.
9. Ganeshalingam S, Rajeswaran G, Jones RL, Thway K, Moskovic E. Leiomyosarcomas of the inferior vena cava: diagnostic features on cross-sectional imaging. Clin Radiol 2011;66(1):50–56.
10. Hartman DS, Hayes WS, Choyke PL, Tibbetts GP. From the archives of the AFIP: leiomyosarcoma of the retroperitoneum and inferior vena cava—radiologic-pathologic correlation. RadioGraphics 1992;12(6):1203–1220.
11. Bathan AJ, Constantinidou A, Pollack SM, Jones RL. Diagnosis, prognosis, and management of leiomyosarcoma: recognition of anatomic variants. Curr Opin Oncol 2013;25(4):384–389.
12. Schaefer IM, Fletcher CD. Diagnostically challenging spindle cell neoplasms of the retroperitoneum. Surg Pathol Clin 2015;8(3):353–374.
13. Guillou L, Coindre JM, Bonichon F, et al. Comparative study of the National Cancer Institute and French Federation of Cancer Centers Sarcoma Group grading systems in a population of 410 adult patients with soft tissue sarcoma. J Clin Oncol 1997;15(1):350–362.
14. Coindre JM. Grading of soft tissue sarcomas: review and update. Arch Pathol Lab Med 2006;130(10):1448–1453.
15. Hasegawa T. Histological grading and MIB-1 labeling index of soft-tissue sarcomas. Pathol Int 2007;57(3):121–125.
16. Guillou L, Aurias A. Soft tissue sarcomas with complex genomic profiles. Virchows Arch 2010;456(2):201–217.
17. Wang R, Titley JC, Lu YJ, et al. Loss of 13q14-q21 and gain of 5p14-pter in the progression of leiomyosarcoma. Mod Pathol 2003;16(8):778–785.
18. Kratz CP, Achatz MI, Brugières L, et al. Cancer screening recommendations for individuals with Li-Fraumeni syndrome. Clin Cancer Res 2017;23(11):e38–e45.
19. Kleinerman RA, Schonfeld SJ, Tucker MA. Sarcomas in hereditary retinoblastoma. Clin Sarcoma Res 2012;2(1):15.
20. Strauss DC, Hayes AJ, Thomas JM. Retroperitoneal tumours: review of management. Ann R Coll Surg Engl 2011;93(4):275–280.
21. National Comprehensive Cancer Network. NCCN soft tissue sarcoma guidelines. Version 2.2018. https://www.nccn.org/professionals/physician_gls/pdf/sarcoma.pdf. Accessed April 17, 2018.
22. Trans-Atlantic RPS Working Group. Management of primary retroperitoneal sarcoma (RPS) in the adult: a consensus approach from the Trans-Atlantic RPS Working Group. Ann Surg Oncol 2015;22(1):256–263.

23. Strauss DC, Hayes AJ, Thway K, Moskovic EC, Fisher C, Thomas JM. Surgical management of primary retroperitoneal sarcoma. Br J Surg 2010;97(5):698–706.
24. Manzella A, Borba-Filho P, D'Ippolito G, Farias M. Abdominal manifestations of lymphoma: spectrum of imaging features. ISRN Radiol 2013;2013:483069.
25. Yu RS, Zhang WM, Liu YQ. CT diagnosis of 52 patients with lymphoma in abdominal lymph nodes. World J Gastroenterol 2006;12(48):7869–7873.
26. Sarkar R, Paul R, Sengupta A, Das I, Mondal J, Panigrahi A. Floating aorta sign. J Assoc Physicians India 2016;64 (12):74.
27. Farid M, Ong WS, Tan MH, et al. The influence of primary site on outcomes in leiomyosarcoma: a review of clinicopathologic differences between uterine and extrauterine disease. Am J Clin Oncol 2013;36(4):368–374.
28. Kreydin EI, Barrisford GW, Feldman AS, Preston MA. Testicular cancer: what the radiologist needs to know. AJR Am J Roentgenol 2013;200(6):1215–1225.
29. Paño B, Sebastià C, Buñesch L, et al. Pathways of lymphatic spread in male urogenital pelvic malignancies. RadioGraphics 2011;31(1):135–160.
30. Husband JE. CT/MRI of nodal metastases in pelvic cancer. Cancer Imaging 2015;2(2):123–129.
31. Shaaban AM, Rezvani M, Tubay M, Elsayes KM, Woodward PJ, Menias CO. Fat-containing retroperitoneal lesions: imaging characteristics, localization, and differential diagnosis. RadioGraphics 2016;36(3):710–734.
32. Rha SE, Byun JY, Jung SE, Chun HJ, Lee HG, Lee JM. Neurogenic tumors in the abdomen: tumor types and imaging characteristics. RadioGraphics 2003;23(1):29–43.
33. Levy AD, Patel N, Dow N, Abbott RM, Miettinen M, Sobin LH. From the archives of the AFIP: abdominal neoplasms in patients with neurofibromatosis type 1—radiologic-pathologic correlation. RadioGraphics 2005;25(2):455–480.
34. Lonergan GJ, Schwab CM, Suarez ES, Carlson CL. Neuroblastoma, ganglioneuroblastoma, and ganglioneuroma: radiologic-pathologic correlation. RadioGraphics 2002;22(4):911–934.
35. Lee KY, Oh YW, Noh HJ, et al. Extraadrenal paragangliomas of the body: imaging features. AJR Am J Roentgenol 2006; 187(2):492–504.
36. Lussey-Lepoutre C, Buffet A, Gimenez-Roqueplo AP, Favier J. Mitochondrial deficiencies in the predisposition to paraganglioma. Metabolites 2017;7(2):E17.
37. Hayes WS, Davidson AJ, Grimley PM, Hartman DS. Extraadrenal retroperitoneal paraganglioma: clinical, pathologic, and CT findings. AJR Am J Roentgenol 1990;155(6): 1247–1250.
38. Sudour-Bonnange H, Faure-Conter C, Martelli H, et al. Primary mediastinal and retroperitoneal malignant germ cell tumors in children and adolescents: results of the TGM95 trial, a study of the French Society of Pediatric Oncology (Société Française des Cancers de l'Enfant). Pediatr Blood Cancer 2017;64(9):e26494.
39. Peterson CM, Buckley C, Holley S, Menias CO. Teratomas: a multimodality review. Curr Probl Diagn Radiol 2012;41(6): 210–219.
40. Smillie RP, Shetty M, Boyer AC, Madrazo B, Jafri SZ. Imaging evaluation of the inferior vena cava. RadioGraphics 2015;35(2):578–592.
41. Yang DM, Jung DH, Kim H, et al. Retroperitoneal cystic masses: CT, clinical, and pathologic findings and literature review. RadioGraphics 2004;24(5):1353–1365.
42. Goenka AH, Shah SN, Remer EM. Imaging of the retroperitoneum. Radiol Clin North Am 2012;50(2):333–355, vii.
43. Cohan RH, Shampain KL, Francis IR, et al. Imaging appearance of fibrosing diseases of the retroperitoneum: can a definitive diagnosis be made? Abdom Radiol (NY) 2018;43 (5):1204–1214.
44. Runowska M, Majewski D, Puszczewicz M. Retroperitoneal fibrosis: the state-of-the-art. Reumatologia 2016;54(5): 256–263.
45. Elsayes KM, Staveteig PT, Narra VR, Chen ZM, Moustafa YL, Brown J. Retroperitoneal masses: magnetic resonance imaging findings with pathologic correlation. Curr Probl Diagn Radiol 2007;36(3):97–106.
46. Zhou LP, Zhang B, Peng WJ, Yang WT, Guan YB, Zhou KR. Imaging findings of Castleman disease of the abdomen and pelvis. Abdom Imaging 2008;33(4):482–488.
47. Bonekamp D, Horton KM, Hruban RH, Fishman EK. Castleman disease: the great mimic. RadioGraphics 2011;31 (6):1793–1807.
48. Kim TJ, Han JK, Kim YH, Kim TK, Choi BI. Castleman disease of the abdomen: imaging spectrum and clinicopathologic correlations. J Comput Assist Tomogr 2001;25(2):207–214.