Leiomyomas beyond the Uterus: Unusual Locations, Rare Manifestations[1]

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LEARNING OBJECTIVES

After reading this article and taking the test, the reader will be able to:

- Describe the unusual sites and uncommon growth patterns of extrauterine leiomyomas.
- Identify the clinical manifestations that are distinctive to leiomyomas.
- Recognize the spectrum of imaging findings that help guide the diagnosis and management of extrauterine leiomyomas.

TEACHING POINTS

See last page

Uterine leiomyomas affect 20%–30% of women older than 35 years. Extrauterine leiomyomas are rarer, and they present a greater diagnostic challenge: These histologically benign tumors, which originate from smooth muscle cells, usually arise in the genitourinary tract (in the vulva, ovaries, urethra, and urinary bladder) but may arise in nearly any anatomic site. In addition, unusual growth patterns may be seen, including benign metastasizing leiomyoma, disseminated peritoneal leiomyomatosis, intravenous leiomyomatosis, parasitic leiomyoma, and retroperitoneal growth. In the presence of such a pattern, a synchronous uterine leiomyoma or a previous hysterectomy for removal of a primary uterine tumor may be indicative of the diagnosis. However, some extrauterine leiomyomas may mimic malignancies, and serious diagnostic errors may result. The most useful modalities for detecting extrauterine leiomyomas are ultrasonography, computed tomography, and magnetic resonance (MR) imaging. The superb contrast resolution and multiplanar capabilities of MR imaging make it particularly valuable for characterizing these tumors, which usually show low signal intensity similar to that of smooth muscle on T2-weighted images. The radiologist's recognition of this and other characteristic features may help steer the clinician toward timely, appropriate management and away from unnecessary, potentially harmful treatment.

Abbreviations: IVC = inferior vena cava, SE = spin echo

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Introduction

Leiomyomas represent the most common gynecologic and uterine neoplasms. Approximately 20%–30% of women older than 35 years have uterine leiomyomas that are manifested clinically (1,2). The radiologic diagnosis of classic uterine leiomyomas is straightforward, given their typical imaging features and their common clinical manifestations. However, leiomyomas occasionally occur with unusual growth patterns or in unusual locations that make their identification more challenging both clinically and radiologically. Examples of leiomyomas with an uncommon growth pattern include diffuse peritoneal leiomyomatosis, intravenous leiomyomatosis, benign metastasizing leiomyomas, retroperitoneal leiomyomas, and parasitic leiomyomas. Leiomyomas with a rare growth pattern occur most often in women of reproductive age. A history of hysterectomy or the presence of concurrent uterine leiomyomas may be suggestive of the diagnosis. Diffuse peritoneal leiomyomatosis manifests as innumerable peritoneal nodules resembling those in peritoneal carcinomatosis. Intravenous leiomyomatosis sometimes manifests as serpentine growths within the inferior vena cava (IVC) and other systemic veins and may extend to the heart. Benign metastasizing leiomyoma may manifest as multiple nodules or masses in the lungs or other sites, mimicking metastases from malignant tumors. Parasitic leiomyoma and retroperitoneal leiomyomatosis usually manifest as single or multiple pelvic or retroperitoneal masses. The unusual locations that are described in this article are largely confined to the genitourinary tract (the urinary bladder, urethra, vulva, and ovaries). Knowledge of the unusual and protean imaging manifestations of these almost always benign entities is essential to distinguish them from malignant tumors that may bear a close resemblance.

Teaching Point

Unusual Growth Patterns

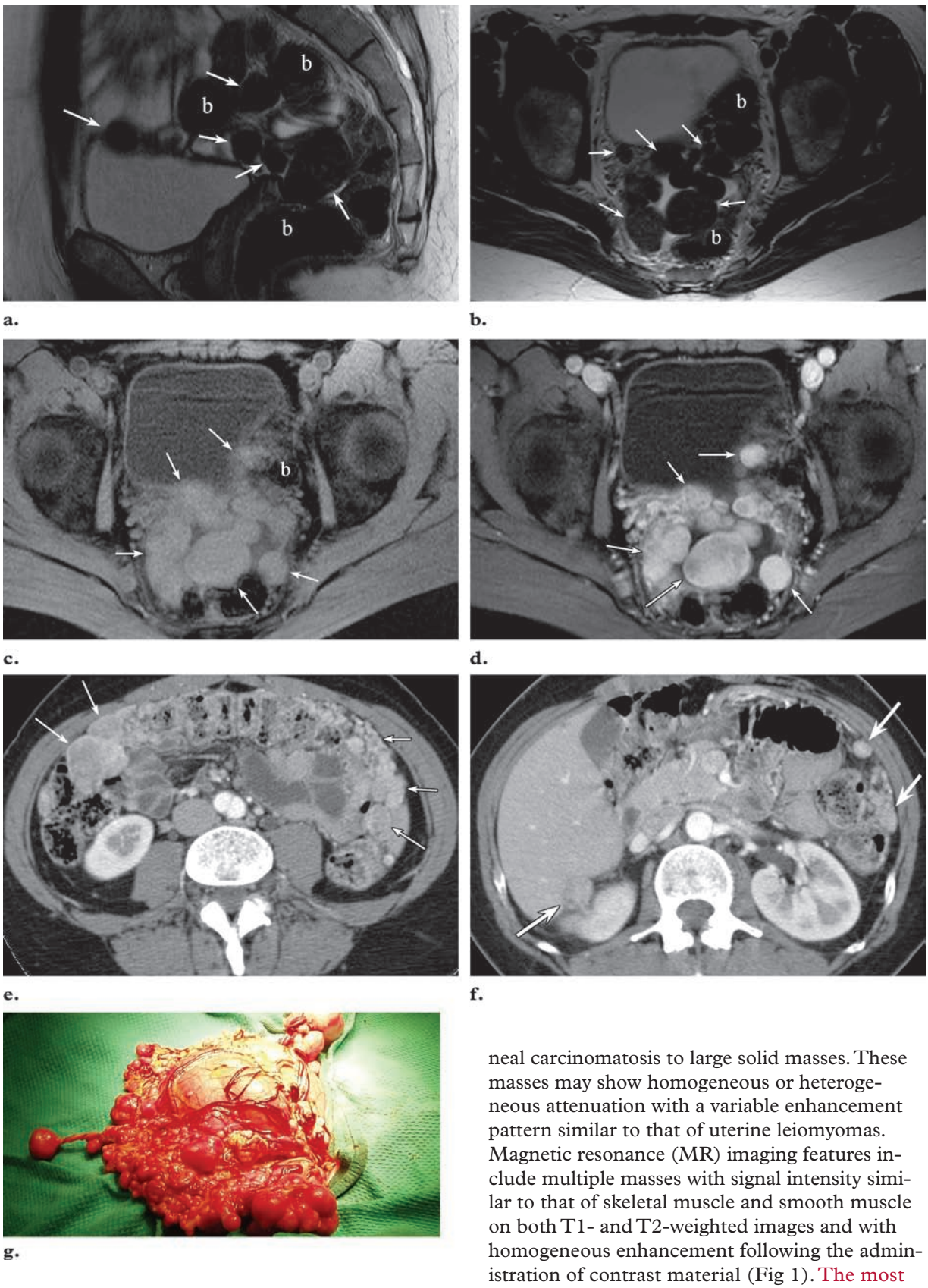
Disseminated peritoneal leiomyomatosis, benign metastasizing leiomyoma, intravenous leiomyomatosis, parasitic leiomyoma, and retroperitoneal leiomyomatosis represent rare exceptions to the usually localized growth pattern of leiomyomas, which most often are confined to the uterus.

Disseminated Peritoneal Leiomyomatosis

Leiomyomatosis peritonealis disseminata is an exceedingly rare benign disorder characterized by multiple vascular leiomyomas growing along the submesothelial tissues of the abdominopelvic peritoneum. First defined by Taubert et al (3), it is usually discovered incidentally in women of reproductive age. More than 100 cases have been described in the English-language literature. Although controversy surrounds the pathogenesis of this disorder, the strong influence of hormonal factors may be deduced from documented associations with pregnancy, long-term use of oral contraceptives, and, occasionally, granulosa cell tumors of the ovary (4–6). Disseminated peritoneal leiomyomatosis has occurred rarely both in men in whom no excess of hormones was identifiable and in postmenopausal women. Such occurrences may be explained in part by the increased responsiveness of tumor cells to normal hormone levels; increases in estrogen and progesterone receptors have been detected in tumors during immunohistochemical analyses and binding assays (7). In women, the tumors often regress after childbirth or the removal of the endogenous or exogenous source of hormone excess (eg, after bilateral oophorectomy). Treatment of uterine leiomyomas with laparoscopic myomectomy has been implicated in the subsequent development of diffuse peritoneal leiomyomatosis due to dissemination of the tumor cells along the laparoscopic tract (8,9).

It is hypothesized that diffuse peritoneal leiomyomatosis is the result of smooth muscle metaplasia in the subcoelomic mesenchyme, the embryologic tissue from which the peritoneal lining and female internal genitalia originate. That hypothesis also might account for the association of diffuse peritoneal leiomyomatosis with endometriosis, as the subcoelomic mesenchyme is thought to be capable of differentiating into various tissues, including endometrial glandular epithelium (6).

Figure 1. Diffuse peritoneal leiomyomatosis in a 46-year-old woman 5 years after a hysterectomy. **(a–c)** Sagittal T2-weighted **(a)**, axial T2-weighted **(b)**, and axial unenhanced T1-weighted fat-suppressed **(c)** fast spin-echo (SE) MR images show several well-defined pelvic nodules (arrows) with low signal intensity similar to that of muscle of the pelvic girdle. Note the absence of the uterus in **a** and the small amount of accumulated fluid between the nodules in **b**. *b* = bowel. **(d)** Axial contrast-enhanced T1-weighted fat-suppressed fast SE MR image depicts homogeneous enhancement of the lesions (arrows). **(e, f)** Axial contrast-enhanced CT images (**e** at a level lower than **f**) obtained to exclude an intraabdominal malignancy (peritoneal carcinomatosis) demonstrate widespread enhancing nodules (arrows) throughout the peritoneal recesses and mesentery but no evidence of a primary tumor or of ascites. **(g)** Photograph obtained during subsequent debulking laparotomy and salpingo-oophorectomy shows innumerable leiomyomas extending along the peritoneum. (Fig 1g courtesy of Michael Fung Kee Fung, MD.)



Ultrasonography (US) and computed tomography (CT) in patients with this condition reveal a spectrum of features ranging from multiple solid subcentimetric nodules like those in peritoneal carcinomatosis to large solid masses. These masses may show homogeneous or heterogeneous attenuation with a variable enhancement pattern similar to that of uterine leiomyomas. Magnetic resonance (MR) imaging features include multiple masses with signal intensity similar to that of skeletal muscle and smooth muscle on both T1- and T2-weighted images and with homogeneous enhancement following the administration of contrast material (Fig 1). The most important entity in the differential diagnosis of diffuse peritoneal leiomyomatosis is peritoneal carcinomatosis, which typically manifests with weight loss, ascites, and disease progression observed at imaging. By contrast, the absence of

Teaching Point

clinical symptoms and of a known primary malignancy characterized by insidious, asymptomatic development is suggestive of a benign cause such as diffuse peritoneal leiomyomatosis (10). Other entities that should be included in the differential diagnosis include primary peritoneal mesothelioma, lymphoma, tuberculosis, and desmoid tumors. Mesothelioma is commonly seen in middle-aged men and, because of its insidious nature, is usually advanced at the initial manifestation, with extensive plaques and masses, and with or without direct invasion of the liver, pancreas, bladder, and bowel (11). The fibrotic type of peritoneal tuberculosis usually can be differentiated by the observation of hypoattenuating features that are representative of associated necrotic mesenteric lymphadenopathy (12). Findings of predominant retroperitoneal lymphadenopathy and homogeneously attenuating, nonnecrotic, noncalcified lymph nodes favor a diagnosis of untreated lymphoma.

Exploratory laparotomy and surgical biopsy often are required for a definitive diagnosis of diffuse peritoneal leiomyomatosis. However, even before surgery, the results of an imaging-guided percutaneous biopsy may be suggestive or indicative of the diagnosis. The benign nodules lack mitotic activity and atypia, which are characteristic features of leiomyosarcoma. Differentiation of diffuse peritoneal leiomyomatosis from leiomyosarcoma is also possible at positron emission tomography with fluorine 18 fluorodeoxyglucose, the most useful diagnostic imaging method for this purpose. The standardized uptake value (SUV) of leiomyomas is negative; if the SUV is positive, the presence of sarcomatous transformation is likely (13). Unlike other pelvic malignancies, many uterine sarcomas have an SUV of less than 2.5 (13).

Therapeutic options include medical or surgical castration with or without resection of leiomyomatous implants. The clinical course is almost invariably benign; however, sarcomatous transformation has been reported (14–16). Therefore, close surveillance is mandatory.

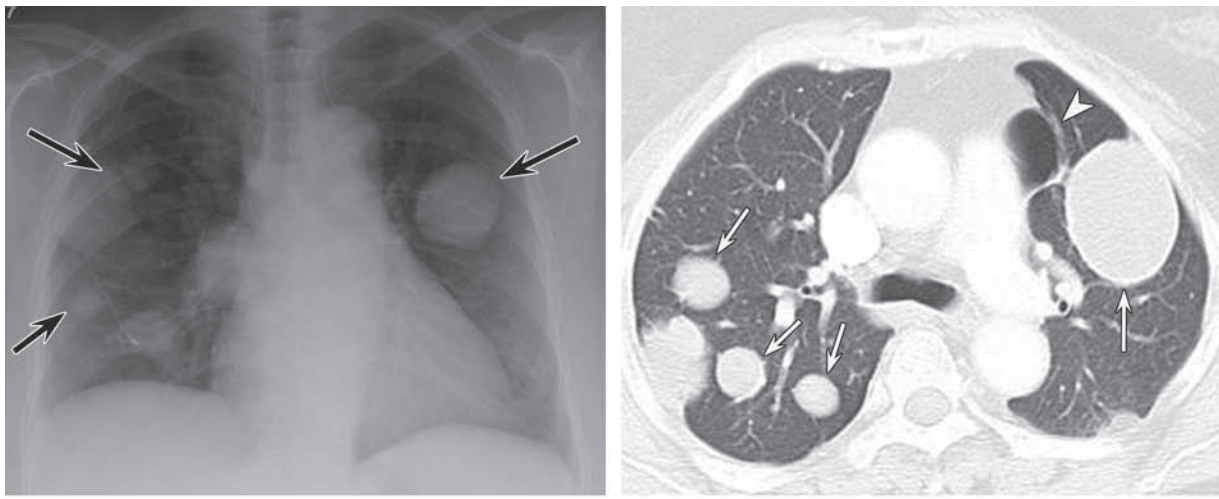
Benign Metastasizing Leiomyoma

This rare condition is characterized by numerous well-differentiated leiomyomas at sites distant from the uterus. The lesions are histologically identical to their uterine counterparts. Since the condition was first described by Steiner in 1939 (17), 120 cases have been documented in the literature. Metastases most often affect the lungs (18), whereas the heart, brain, lymph nodes, bone, and skin are more rarely affected. The condition usually manifests as multiple incidentally detected pulmonary nodules in middle-aged women. A history of hysterectomy for uterine leiomyoma may be indicative, with the mean reported interval between hysterectomy and the appearance of pulmonary nodules ranging from 3 months to 20 years. A previous diagnosis of uterine leiomyoma may point to the diagnosis in many cases. Occasional cases of metastasizing leiomyoma also have been reported in male patients (18,19). Symptoms of chest pain, shortness of breath, and cough have been described. Although the clinical course is usually indolent, a more rapid progression to severe respiratory symptoms also has been reported (20).

It is now largely accepted that the lesions arise as hematogenous metastases from benign tumors; however, a second school of thought still supports a hypothesis of multiple independent foci of smooth muscle proliferation. The primary uterine lesions are classified as smooth muscle tumors of unknown malignant potential because of the limitations of current histopathologic tests. Associations with diffuse peritoneal leiomyomatosis (21), intravenous leiomyomatosis (22), and diffuse uterine leiomyomatosis (23) have been observed and may be indicative of a common pathologic origin.

Teaching Point

The radiologic imaging appearance of pulmonary nodules in benign metastasizing leiomyomas varies from solitary subcentimetric lesions to multiple lesions mimicking pulmonary metastases from malignant tumors (Fig 2). Cavitation of lesions occasionally takes place (Fig 2c) and rarely may be accompanied by pneumothorax.



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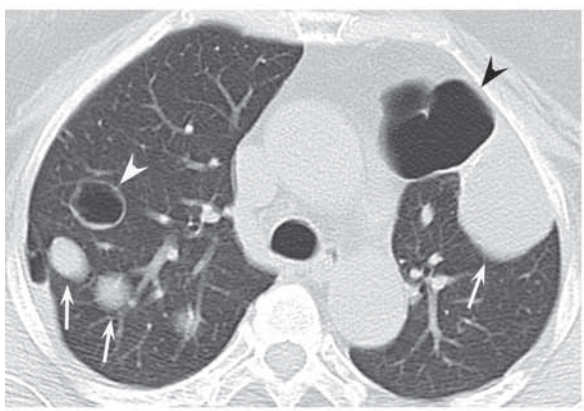


c.

Figure 2. Benign metastasizing leiomyoma in a 50-year-old woman 10 years after a hysterectomy for treatment of uterine fibroids. The condition was diagnosed at open lung biopsy at another institution. **(a)** Frontal chest radiograph demonstrates multiple lung masses (arrows) indistinguishable from metastases. **(b)** Axial unenhanced CT image depicts bilateral pulmonary masses (arrows) and a bulla in the left lung (arrowhead). **(c)** Axial unenhanced CT image, obtained 4 years after the initial diagnosis, shows stability in the size of the nodules (arrows) and some evidence of cavitation (white arrowhead). The bulla (black arrowhead) has enlarged. The patient remained asymptomatic at the most recent follow-up evaluation.

Calcification is rare. Occasional cases with a miliary pattern (24) and a pattern simulating interstitial lung disease (25) have been documented. Both CT and MR imaging may be used to depict the pulmonary nodules in benign metastasizing leiomyoma, which have a nonspecific appearance and usually enhance homogeneously. The inclusion of particular entities in the differential diagnosis depends on the size of the nodules, but the most commonly included are metastases from malignant tumors (22). Less common entities to consider are infectious granulomas, sarcoidosis, rheumatoid nodules, and amyloidosis. An imaging-guided core biopsy is frequently required to obtain a definitive diagnosis. As in diffuse peritoneal leiomyomatosis, estrogen and progesterone receptors have been identified in these metastatic foci; the response to hormonal influences therefore may be similar to that observed in diffuse peritoneal leiomyomatosis. Spontaneous resolution of benign metastasizing leiomyoma has been described (26,27).

Intravenous Leiomyomatosis

Teaching Point

Intravenous leiomyomatosis—a rare disease that is histologically benign but clinically aggressive—is characterized by the intraluminal growth of leiomyomas in intrauterine and systemic veins. These lesions are implants from coexistent or previously resected uterine fibroids. Fewer than 150

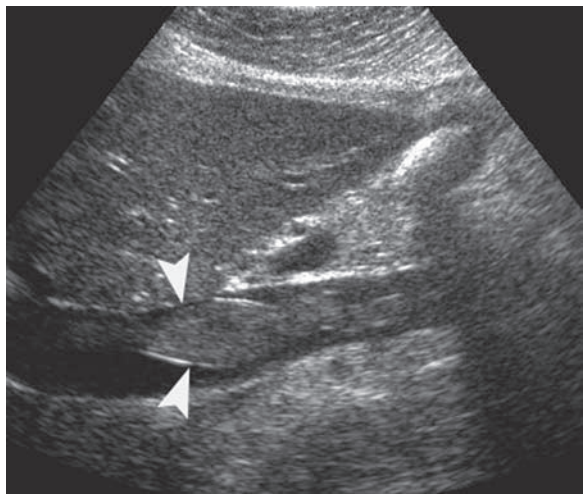
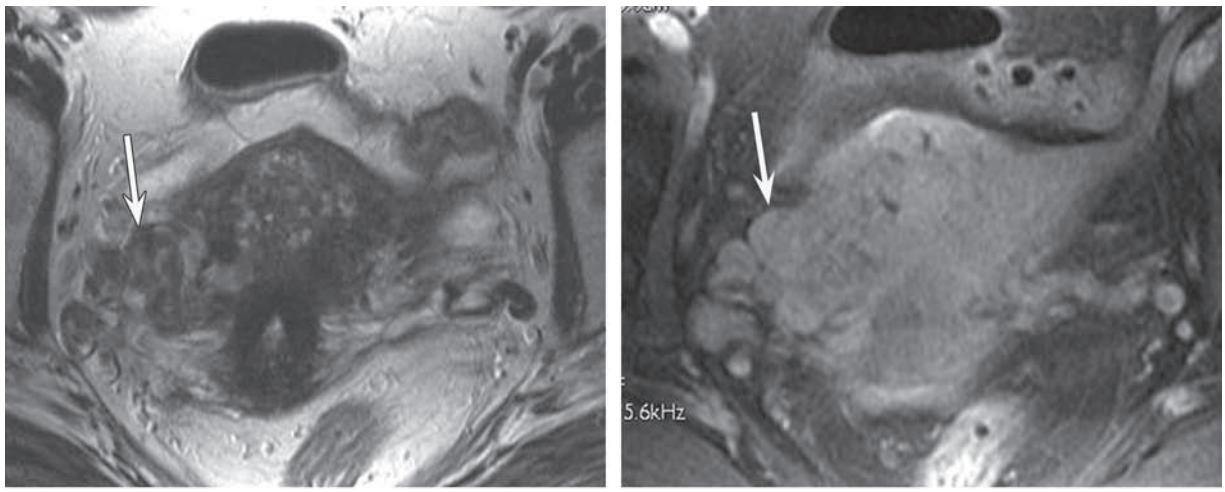


Figure 3. Benign intracaval leiomyomatosis in a 38-year-old asymptomatic woman with a history of hysterectomy for treatment of multiple uterine leiomyomas. Sagittal gray-scale US image demonstrates an accumulation of nonocclusive echogenic material (arrowheads) within the infra- and intrahepatic segments of the IVC. No intraabdominal malignancy was visible at cross-sectional imaging. The patient did not respond to anticoagulant drug therapy, and the cordlike solid lesions were surgically excised. The diagnosis was based on pathologic analysis.

cases of intravenous leiomyomatosis are described in the literature. Tumor growth into the venous channels of the myometrium and parametrium occurs in an estimated 80% of cases, and cardiac involvement is seen in 10%–40% of cases (28,29).

The clinical course is variable and depends on the burden of disease. The vascular smooth muscle tumors may extend into the great veins and even the right atrium of the heart, where they may cause a fatal obstruction. US images usually demonstrate vascularized thrombi within the pelvic veins and IVC (Fig 3). Extension into the right atrium may be adequately assessed with echocardiography; CT and MR imaging, with their multiplanar capabilities, may demonstrate continuity in intraluminal tumor growth from the pelvic veins (Fig 4). The appearance of the lesions on MR images depends on the amounts of smooth muscle cells and fibrous tissue that each lesion contains. The typical appearance is low to intermediate signal intensity on T1-weighted images and low signal intensity on T2-weighted images. The most important entity to be considered in the differential diagnosis is leiomyosarcoma arising from the wall of the IVC (30). Leiomyosarcoma cannot be differentiated from leiomyoma on the basis of imaging findings alone, unless it has progressed to an advanced stage with visible infiltration and invasion of the abdominal viscera. Other conditions that may simulate leiomyomatosis include bland thrombi within the IVC or other systemic veins. A bland thrombus, like a leiomyoma, may have variable signal intensity on MR images, but it is distinguishable from a leiomyoma by its lack of enhancement following the administration of gadolinium-based contrast material. On US images, a bland thrombus may not be distinguishable from a leiomyoma unless a Doppler measurement of vascularity is performed. A malignant thrombus formed by metastatic renal cell carcinoma, or Wilms tumor, is easily differentiated if the primary tumor is visible at imaging. The presence of coexistent uterine fibroids or a history of surgery for uterine fibroids is highly suggestive of intravenous leiomyomatosis.

Successful clinical management is dependent on total surgical excision, which may necessarily include cardiotomy. The long-term prognosis is good because the growths are hormonally responsive. Preoperative hormonal therapy with antiestrogenic drugs that includes but is not limited to leuprolide has been shown to reduce the disease burden in cases of extensive inoperable tumors. Such therapy facilitates subsequent debulking surgery (31). However, tumors recur in as many as 30% of cases, and long-term follow-



a. b.

Figure 4. Intravenous leiomyomatosis in a 40-year-old woman with a previous diagnosis of multiple uterine leiomyomas. Axial T2-weighted **(a)** and axial contrast-enhanced T1-weighted **(b)** fast SE images of the pelvis show serpentine, cordlike growths (arrow) within the lumina of the parametrial veins. The lesions have low to intermediate signal intensity in **a** and show enhancement similar to that of the adjacent myometrium in **b**.

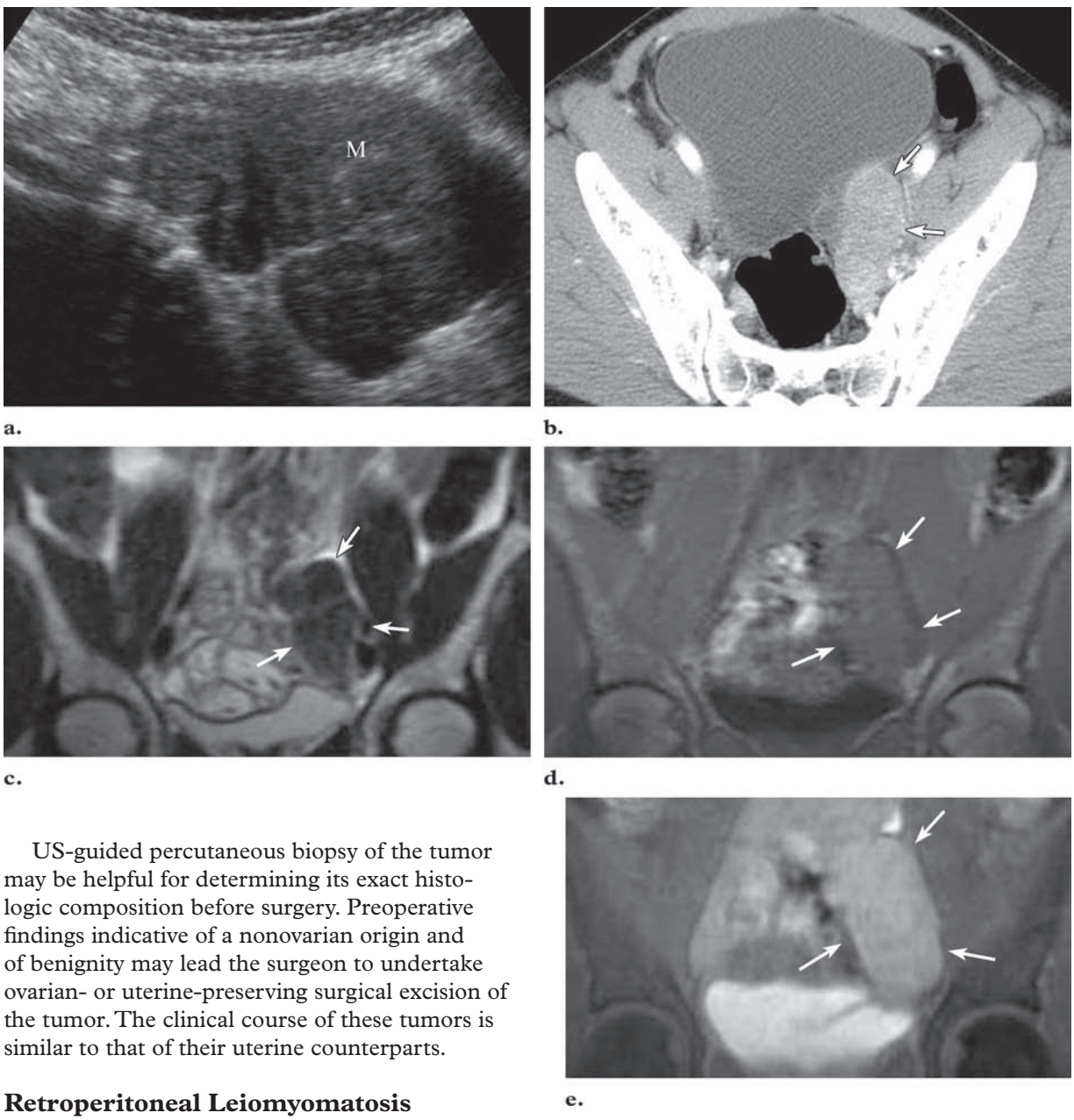
up imaging at 3- to 6-month intervals is necessary (32,33).

Parasitic (Broad Ligament) Leiomyoma

Occasionally, leiomyomas become adherent to surrounding structures (eg, the broad ligament, omentum, or retroperitoneal connective tissue), develop an auxiliary blood supply, and lose their original attachment to the uterus, thus becoming "parasitic." It also has been suggested that leiomyomas that are adherent to the broad ligament originate from hormonally sensitive smooth muscle elements of that ligament (34). Clinically, these lesions may manifest as extrauterine pelvic masses that compress the urethra, bladder neck, or ureter, producing symptoms of varying degrees of urinary outflow obstruction or secondary hydroureteronephrosis.

At US, a typical leiomyoma usually has a whorled appearance, with variable echogenicity depending on the extent of degeneration, fibrosis, and calcification. The differential diagnosis for parasitic leiomyomas includes masses of ovarian origin (both primary neoplasms and metastases), broad ligament cysts, and lymphadenopathy. Transvaginal US may be of great help in diagnosing broad ligament leiomyomas because it allows clear visual separation of the uterus and ovaries from the mass. MR imaging, with its multiplanar imaging capabilities, also may be extremely useful for differentiating broad ligament leiomyomas from masses of ovarian or tubal origin and from broad ligament cysts. The distinctive MR imaging appearances of typical leiomyomas also are useful in differentiating them from solid malignant pelvic tumors. This observation is important because broad ligament leiomyomas are associated with pseudo–Meigs syndrome and produce an elevated CA-125 level that may clinically mimic that in metastatic ovarian carcinoma, thereby causing diagnostic confusion (35). Typical leiomyomas demonstrate low to intermediate signal intensity on T1-weighted images and low signal intensity on T2-weighted images (Fig 5). Myxoid degeneration and necrosis may be visible as high-signal-intensity areas on T2-weighted images. Another common variant seen on both T1- and T2-weighted images is a cobblestone-like appearance due to hyaline degeneration, with high-signal-intensity foci representing areas of infarction due to rapid growth (36,37).

Figure 5. Parasitic leiomyoma in a 56-year-old woman with a remote history of hysterectomy for uterine fibroids. **(a)** Sagittal US image of the left lower quadrant demonstrates a well-defined homogeneous isoechoic mass *(M)* along the wall of the left side of the pelvis. **(b)** Axial contrast-enhanced CT image of the pelvis shows the same homogeneous left pelvic mass (arrows). At surgery, feeding vessels were found that branched from the internal iliac artery. **(c)** Coronal T2-weighted fast SE MR image of the pelvis demonstrates homogeneously hypointense signal in the mass (arrows). **(d)** Coronal unenhanced T1-weighted fast SE MR image of the pelvis demonstrates signal in the mass (arrows) that is isointense to that in the pelvic muscles. **(e)** Coronal contrast-enhanced T1-weighted fat-suppressed fast SE MR image of the pelvis demonstrates homogeneous enhancement of the mass (arrows). The diagnosis of parasitic leiomyoma was confirmed at surgical biopsy.

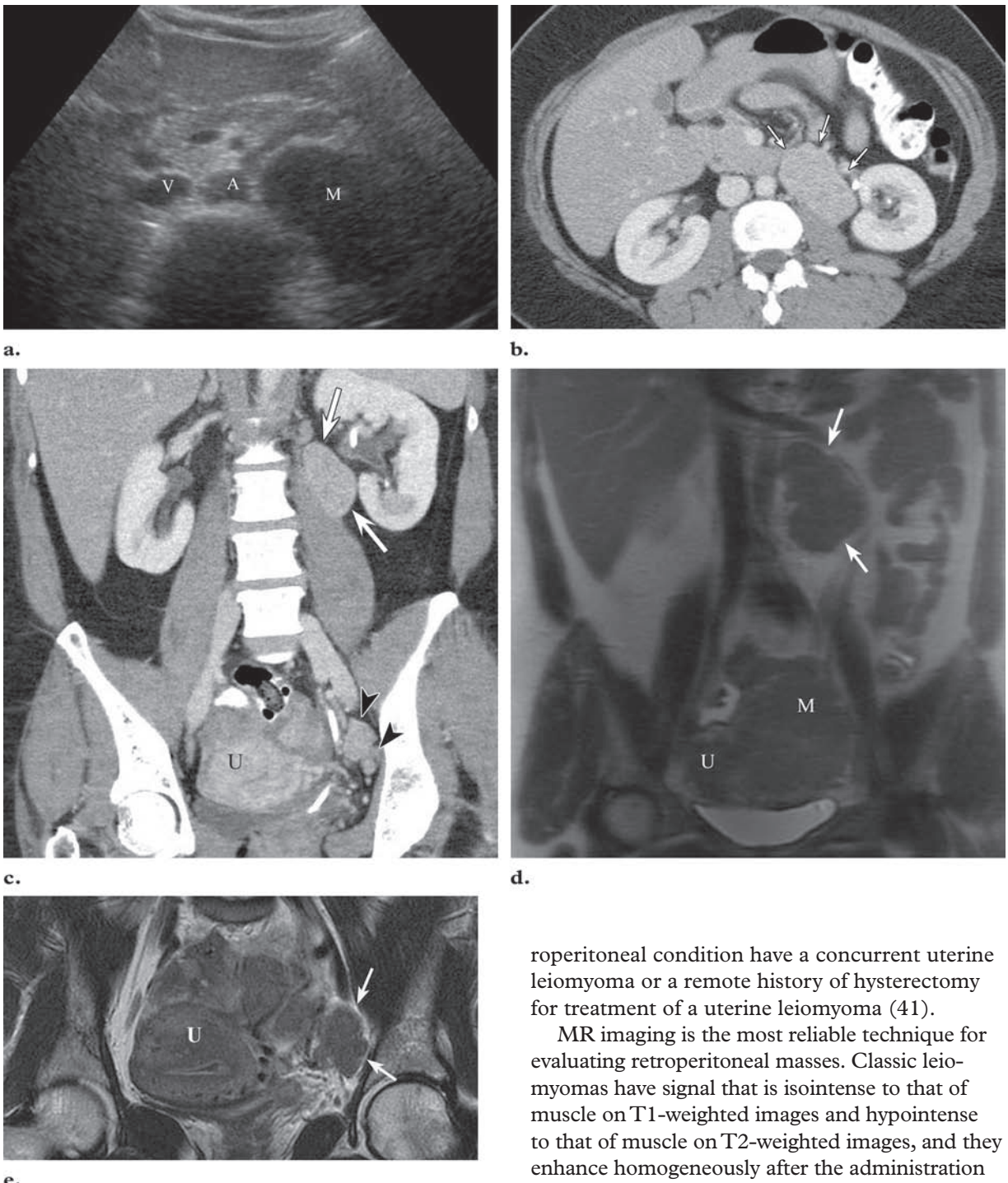


US-guided percutaneous biopsy of the tumor may be helpful for determining its exact histologic composition before surgery. Preoperative findings indicative of a nonovarian origin and of benignity may lead the surgeon to undertake ovarian- or uterine-preserving surgical excision of the tumor. The clinical course of these tumors is similar to that of their uterine counterparts.

Retroperitoneal Leiomyomatosis

Retroperitoneal growth is yet another unusual growth pattern of leiomyomas. Multiple leiomyomatous masses are usually seen in the pelvic retroperitoneum in women with a concurrent uterine leiomyoma or a history of uterine leiomyoma. Rarely, the extrauterine masses may extend to the upper retroperitoneum, as high as the level of the renal hilum. With regard to their pathologic origin, it is unclear whether these retroperitoneal lesions represent metastatic or synchronous primary lesions and whether they arise from the hormonally sensitive smooth muscle elements (38) or from the embryonal remnants of müllerian or wolffian ducts (39). They may enlarge considerably yet remain asymptomatic and be detected incidentally at a routine check-up or autopsy (40). Common symptoms include discomfort, fatigue, and back pain. The lesions are

Figure 6. Retroperitoneal leiomyomatosis in a 38-year-old woman with pelvic pain. **(a)** Transverse US image demonstrates a well-defined hypoechoic mass *(M)* along the left paraaortic recess. *A* = aorta, *V* = vena cava. **(b, c)** Axial **(b)** and coronal **(c)** contrast-enhanced CT images show an enhancing mass lesion in the left-sided retroperitoneum (arrows in **b** and **c**), a smaller solid mass along the left pelvic wall (arrowheads in **c**), and several mass lesions in the enlarged uterus *(U)*. **(d)** Coronal T2-weighted fast SE MR image obtained with a half-Fourier rapid acquisition with relaxation enhancement sequence shows the retroperitoneal mass (arrows) with signal that is isointense to that in muscle. Analysis of a specimen obtained at percutaneous imaging-guided biopsy revealed benign smooth muscle cells with positive staining for estrogen and progesterone receptors, findings indicative of leiomyoma. A large uterine mass *(M)* also is visible. *U* = uterus. **(e)** Coronal T2-weighted fast SE MR image shows the uterus *(U)* and left pelvic mass (arrows), which were surgically resected. The pelvic mass was found to be a broad ligament leiomyoma.



hormonally responsive and have clinical manifestations similar to those of uterine leiomyomas. More than 40% of patients affected by this retroperitoneal condition have a concurrent uterine leiomyoma or a remote history of hysterectomy for treatment of a uterine leiomyoma (41).

MR imaging is the most reliable technique for evaluating retroperitoneal masses. Classic leiomyomas have signal that is isointense to that of muscle on T1-weighted images and hypointense to that of muscle on T2-weighted images, and they enhance homogeneously after the administration of contrast material (Fig 6). US may depict a well-defined mass with a variable but usually homogeneous echotexture within the retroperitoneum.

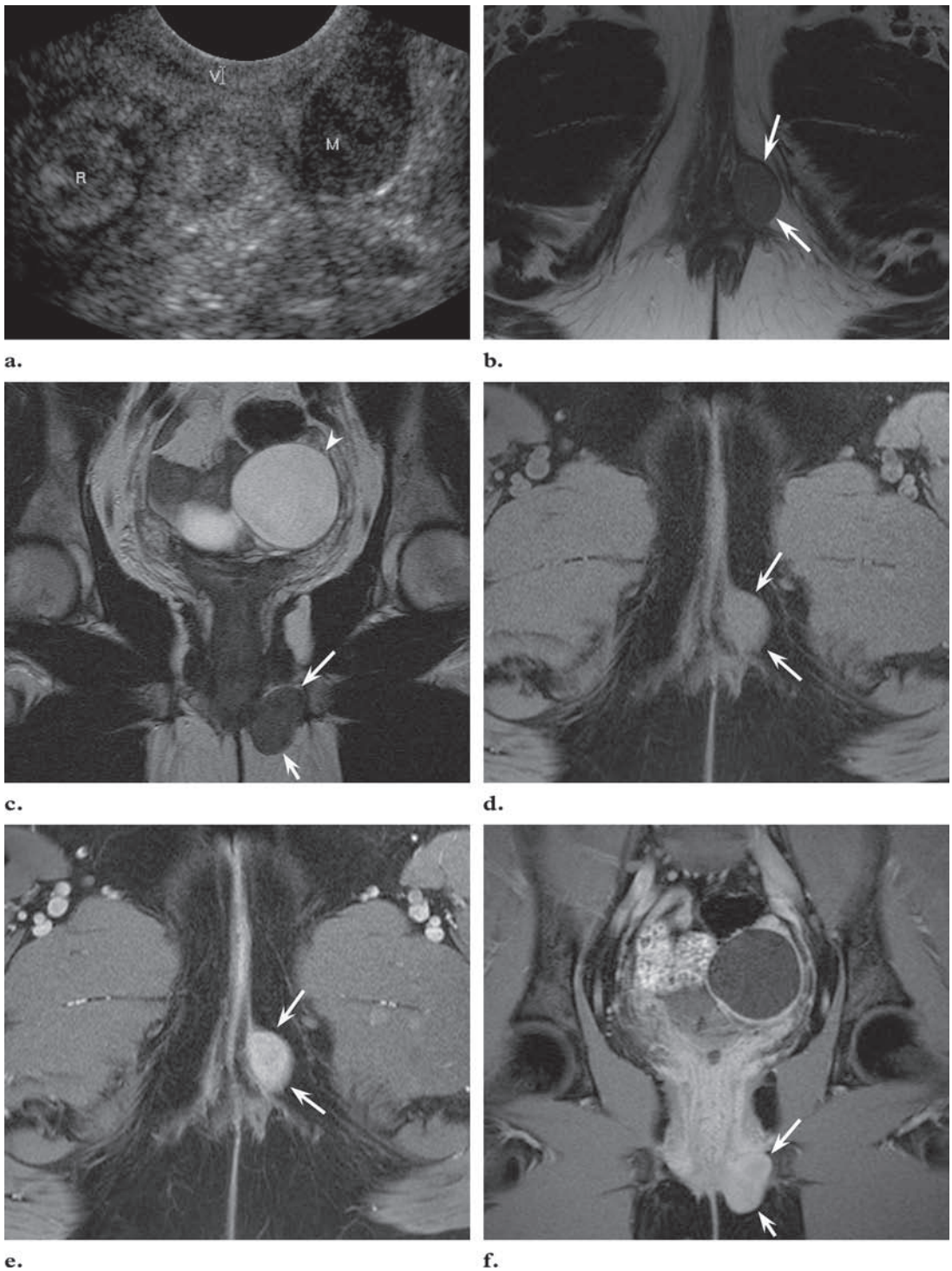


Figure 7. Vulvar leiomyoma in a 46-year-old woman with a previous diagnosis of pelvic endometriosis and a new onset of swelling along the left labium majus. **(a)** Transvaginal US image depicts a hypoechoic mass *(M)* along the left side of the introitus. *R* = rectum, *V* = vagina. **(b, c)** Axial **(b)** and coronal **(c)** T2-weighted fast SE MR images show a low-signal-intensity, well-circumscribed solid vulvar mass (arrows) that appears isointense to the pelvic musculature along the left labial crease. A high-signal-intensity left pelvic lesion (arrowhead in **c**) was depicted incidentally and proved histologically to be an endometrioma. **(d)** Axial unenhanced T1-weighted fat-suppressed fast SE MR image shows the vulvar mass (arrows) with signal that is isointense to that in skeletal muscle. **(e, f)** Axial **(e)** and coronal **(f)** contrast-enhanced T1-weighted fat-suppressed fast SE MR images show homogeneous enhancement in the vulvar mass (arrows), which was confirmed at surgical biopsy to be a leiomyoma.

Homogeneous attenuation is typically seen within the mass at CT.

The differential diagnosis of these retroperitoneal tumors includes common benign and malignant neoplasms of neurogenic origin (schwannoma, paraganglioma, ganglioneuroma, extra-adrenal pheochromocytoma) as well as teratoma, desmoid tumor, hemangioma, extra-adrenal angiomyelolipoma, sarcoma, lymphoma, and metastatic tumors (42). Lipoma and liposarcoma are differentiated by their gross fat content, which is usually well depicted at CT and MR imaging. Smooth muscle tumors within the retroperitoneum are usually malignant. It is not possible to differentiate leiomyoma from leiomyosarcoma on the basis of imaging features alone, although extensive central necrosis, invasive growth, and a heterogeneous appearance are suggestive of leiomyosarcoma; US-guided percutaneous biopsy of the mass is helpful for determining its histologic composition preoperatively. Isolated retroperitoneal leiomyomas and pelvic retroperitoneal leiomyomas are rare occurrences, and the prognosis for patients with these lesions is good (41).

Unusual Locations

Although the uterus is the most common site of origin of leiomyomas, the lesions arise as proliferations of smooth muscle cells, and they may develop at any site where such cells are found. Unusual sites of origin include the vulva, ovaries, urinary bladder, and urethra. Other rare locations, not described in detail in this article, include the sinonasal cavities, orbits, kidneys, and skin. MR imaging is the most useful imaging modality for characterizing these tumors, because, regardless of their anatomic location, classic leiomyomas have signal intensity similar to that of smooth muscle on images obtained with any MR pulse sequence. However, histopathologic analysis is usually required to confirm the diagnosis.

Teaching Point

Vulva

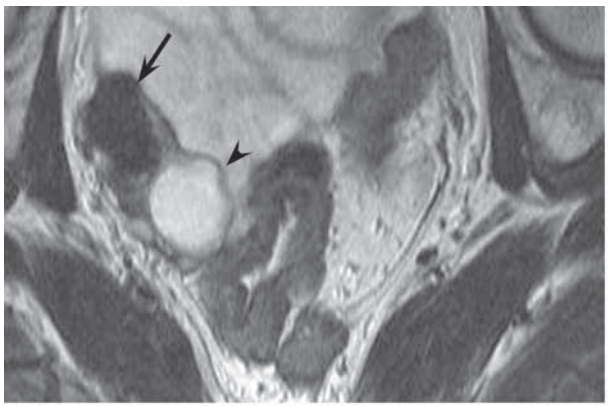
Rarely, extrauterine leiomyomas may be seen along the labia majora. Fewer than 120 cases of smooth muscle tumors of the vulva have been reported in the literature. The lesions may enlarge during pregnancy, and biopsy specimens frequently test positive for estrogen and progesterone receptors at histopathologic analysis. Among those affected by these tumors, the mean age at presentation varies from 13 to 71 years. The average tumor size varies from 0.5 to 15 cm (43). With regard to pathologic origin, the tumors are thought to arise from smooth muscle cells within erectile tissue or blood vessel walls, the round ligament, or, in men, the dartos muscle (44).

Findings at preoperative MR imaging may be suggestive of the benign nature of these tumors. A characteristic finding of low signal intensity mimicking that of smooth muscle on T2-weighted images is the key to diagnosis. The MR signal in the tumors is isointense to that in muscle on T1-weighted images, and the tumors enhance homogeneously after the administration of contrast material (Fig 7). Some tumors—usually, those in pregnant women—exhibit extensive myxoid degeneration, which manifests as intratumoral areas of high signal intensity on T2-weighted images (45). CT may not be of much use in delineating these tumors because of its inherent poor soft-tissue contrast. Percutaneous or surgical biopsy is required for a definitive diagnosis.

The differential diagnosis includes benign and malignant entities such as Bartholin cysts, fibromas, lymphangiomas, soft-tissue sarcomas, and neurogenic tumors. Rarely, Epstein-Barr virus–induced smooth muscle tumors also manifest as vulvar masses in immunocompromised patients (46). Labial leiomyomas are treated with conservative surgery, after which close long-term follow-up is required (43).

Ovary

Primary ovarian leiomyoma is one of the rarest solid tumors of the ovary, constituting only 0.5%–1% of benign ovarian neoplasms (47). Since its first description by Sangralli in 1862, approximately 75 cases have been reported in the English-language medical literature. The tumors most commonly occur in middle-aged women, usually are unilateral, and frequently (80% of cases) are coexistent with uterine leiomyomas (48). Bilateral tumors are usually seen in younger women, in whom coexistent uterine leiomyomas are usually absent (49). Ovarian leiomyomas often are asymptomatic and incidentally detected at surgery or autopsy. However, depending on the size of the tumor, a palpable abdominal mass, ascites, or hydronephrosis may be seen. An association with Meigs syndrome has been described (50).



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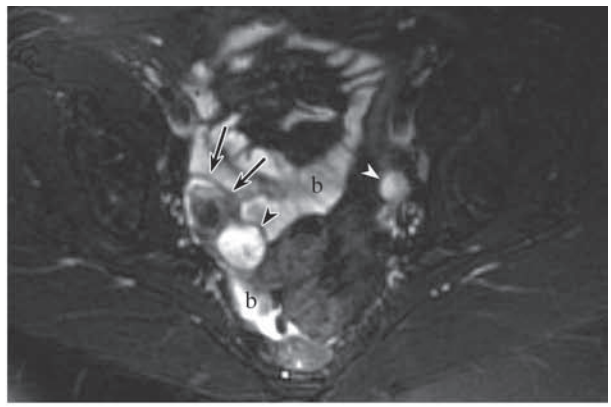

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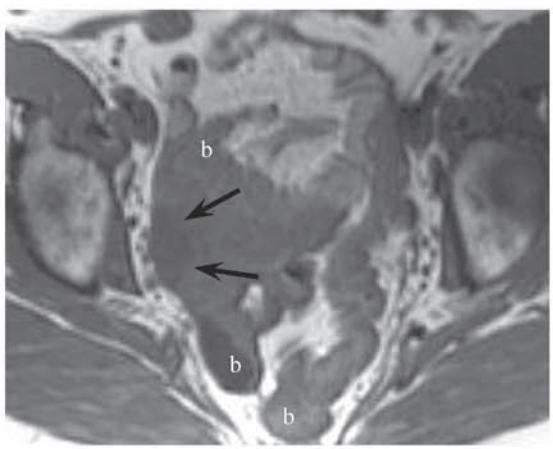

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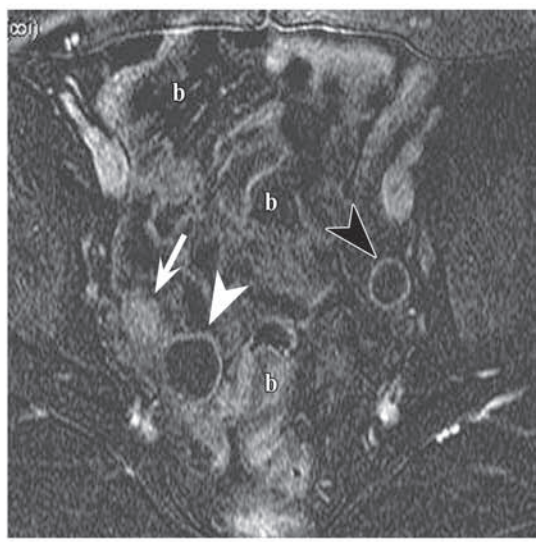

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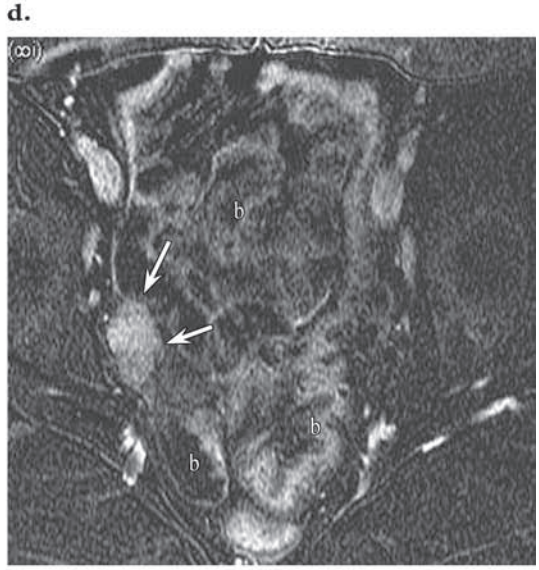


e.

Figure 8. Ovarian leiomyoma in a 49-year-old woman with nonspecific abdominal pain and weight gain after a hysterectomy for treatment of uterine fibroids. The CA-125 level was normal at 13.5 U/mL. *b* = bowel. **(a, b)** Axial oblique non–fat-suppressed **(a)** and axial fat-suppressed **(b)** T2-weighted fast SE MR images demonstrate a low-signal-intensity lesion in the right ovary (arrows) and high-signal-intensity cysts in both ovaries (arrowheads). **(c)** Axial unenhanced non–fat-suppressed T1-weighted fast SE image shows signal in the right ovarian lesion that is iso- or hypointense to that in pelvic muscles (arrows). The cyst is not visible. **(d, e)** Axial contrast-enhanced T1-weighted fat-suppressed fast SE MR images show homogeneous enhancement within the solid lesion (arrows) and the expected fine mural enhancement in the bilateral cysts (arrowheads in **d**). Surgical resection of the right ovary and subsequent histologic analysis helped confirm the presence of a primary ovarian leiomyoma.

The most commonly accepted theory about the pathologic origin of these tumors is that they arise from smooth muscle cells in hilar blood vessels (51). Other potential theories include origin from smooth muscle metaplasia of cortical stroma, ovarian ligaments, and multipotent ovarian stromal cells (52).

MR imaging is potentially useful for the diagnosis of ovarian leiomyomas, which, like uterine leiomyomas, have intermediate signal intensity on T1-weighted images and low signal intensity on T2-weighted images (Fig 8). Ovarian fibroma is the most important entity to consider in the differential diagnosis (53). The early contrast enhancement of leiomyomas may aid in their differentiation from other fibrous ovarian tumors such as fibromas or fibrothecomas, which usually demonstrate delayed weak enhancement (53). The primary ovarian origin of a mass is confirmed either by the absence of a separate ipsilateral ovary or by the presence of small follicles surrounding the mass, features that also may be present in fibromas (54). However, normal ovarian follicles may not be seen, as these tumors are associated with abnormal and at times absent ovarian tissue histologically (55). Secondary involvement of the ovaries, which should not be confused with primary ovarian leiomyoma, may be seen in intravenous leiomyomatosis and leiomyomatosis peritonealis disseminata (56). There are rare reports of extensive cystic degeneration in ovarian vascular leiomyomas, a feature that causes them to closely resemble cystic tumors such as cystadenomas (57).

The usual surgical treatment is oophorectomy, which often is performed with an ovary-preserving technique (enucleation) in young patients. Histopathologic and immunohistochemical studies are performed to obtain a definitive diagnosis. As discussed earlier, the tumors are hormonally responsive, and regression may occur after pregnancy ends (58).

Urethra

Urethral leiomyomas are rare and originate from circular smooth muscle fibers of the urethra. Approximately 120 cases of urethral leiomyomas in female patients have been reported in the English-language medical literature. The tumors primarily occur in women of reproductive age, enlarge during pregnancy, and regress post partum, characteristics that are indicative of their hormonal dependency (59). Occasionally, they occur in males and postmenopausal women (60). Depending on the tumor size, clinical manifestations range from none to bladder outlet obstruction (referred to by some authors as "female pseudoprostate") (61). The most frequent clinical symptom is difficulty in micturition with urinary tract infections (64%), followed by dyspareunia and hematuria (28%) (62). The tumor may manifest as a mass that protrudes into or through the urethra.

The roles of US and MR imaging are to define the morphologic features of the tumor and determine whether it shows any infiltrative behavior, features that may help differentiate it from other entities. As emphasized earlier, the advantages of MR imaging include the ability to evaluate the lesion in multiple planes and to ascertain the anatomic relationships between the lesion, urethra, and vagina—steps that are essential for surgical planning. At US, the tumors appear homogeneous, solid, and smooth walled. A typical whorled appearance may be observed and is useful for preoperative diagnosis. At MR imaging, the tumors have intermediate signal intensity on T1-weighted images and low to intermediate signal intensity on T2-weighted images, features suggestive of their origin from muscle (Fig 9); in addition, they enhance homogeneously after the administration of contrast material.

The differential diagnosis includes urethral and vaginal malignancies, urethral caruncle, urethral diverticulum, urinary bladder leiomyoma, prolapsed ectopic ureterocele, Gartner duct cyst, rhabdomyosarcoma, and malakoplakia. It may be difficult to differentiate between these conditions on the basis of imaging alone, especially because degenerative leiomyomas may include cystic components and therefore may have internal areas of heterogeneous signal intensity. Surgical excision is the standard of treatment. Malignant transformation has not been reported, and local recurrence is rare (63).

Urinary Bladder

Leiomyoma is the most commonly occurring benign neoplasm in the urinary bladder; however, leiomyomas represent only 0.4% of all bladder tumors (64). Approximately 250 cases have been reported in the literature (65). Women in the 3rd to 5th decades of life are predominantly affected (66). Some reports describe equal incidence in male and female patients (67). Leiomyomas may occur in intravesical (51.1%), intramural (30%), and extravesical (16.7%) locations in the bladder (68). The site and dimensions of the tumor

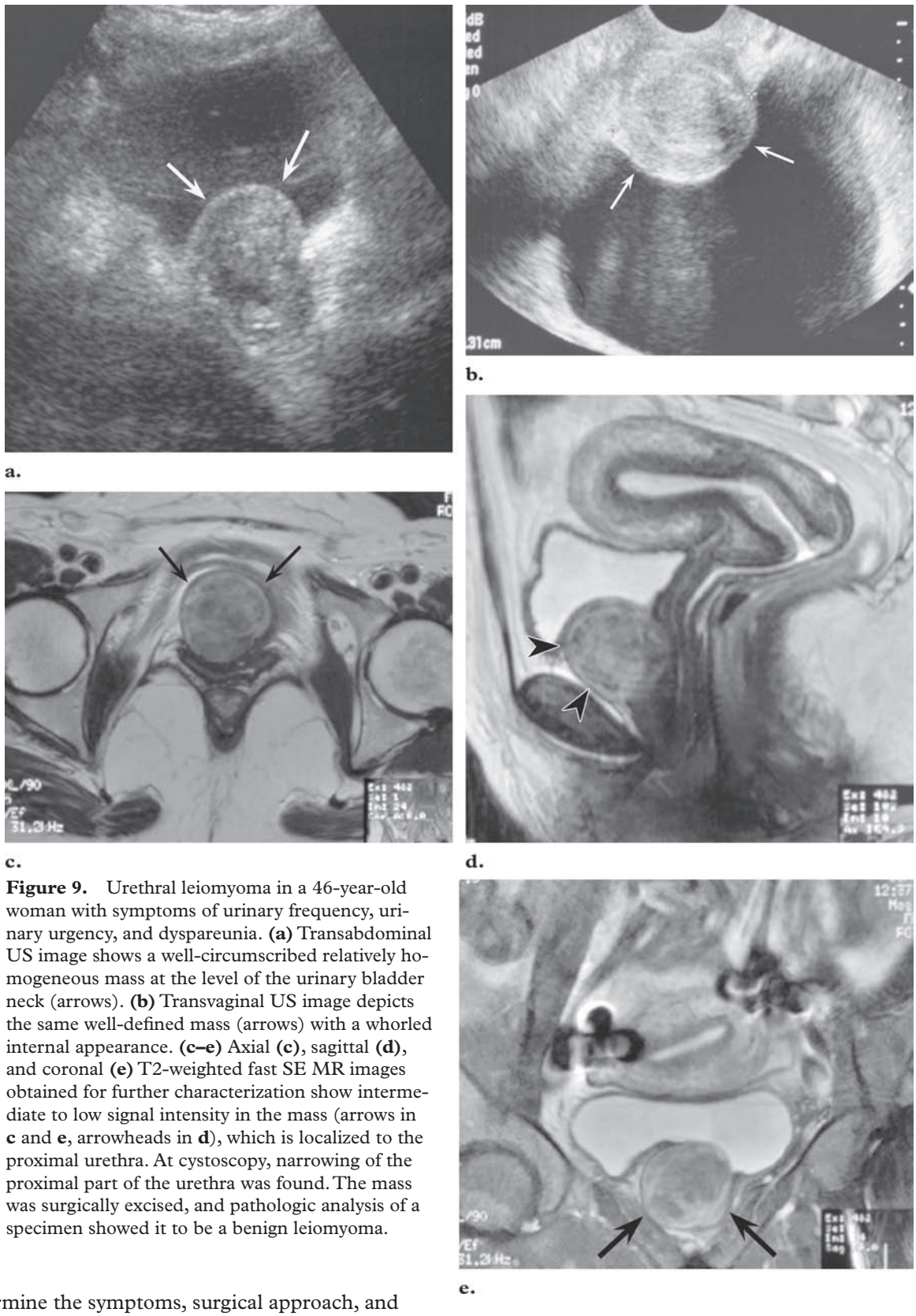
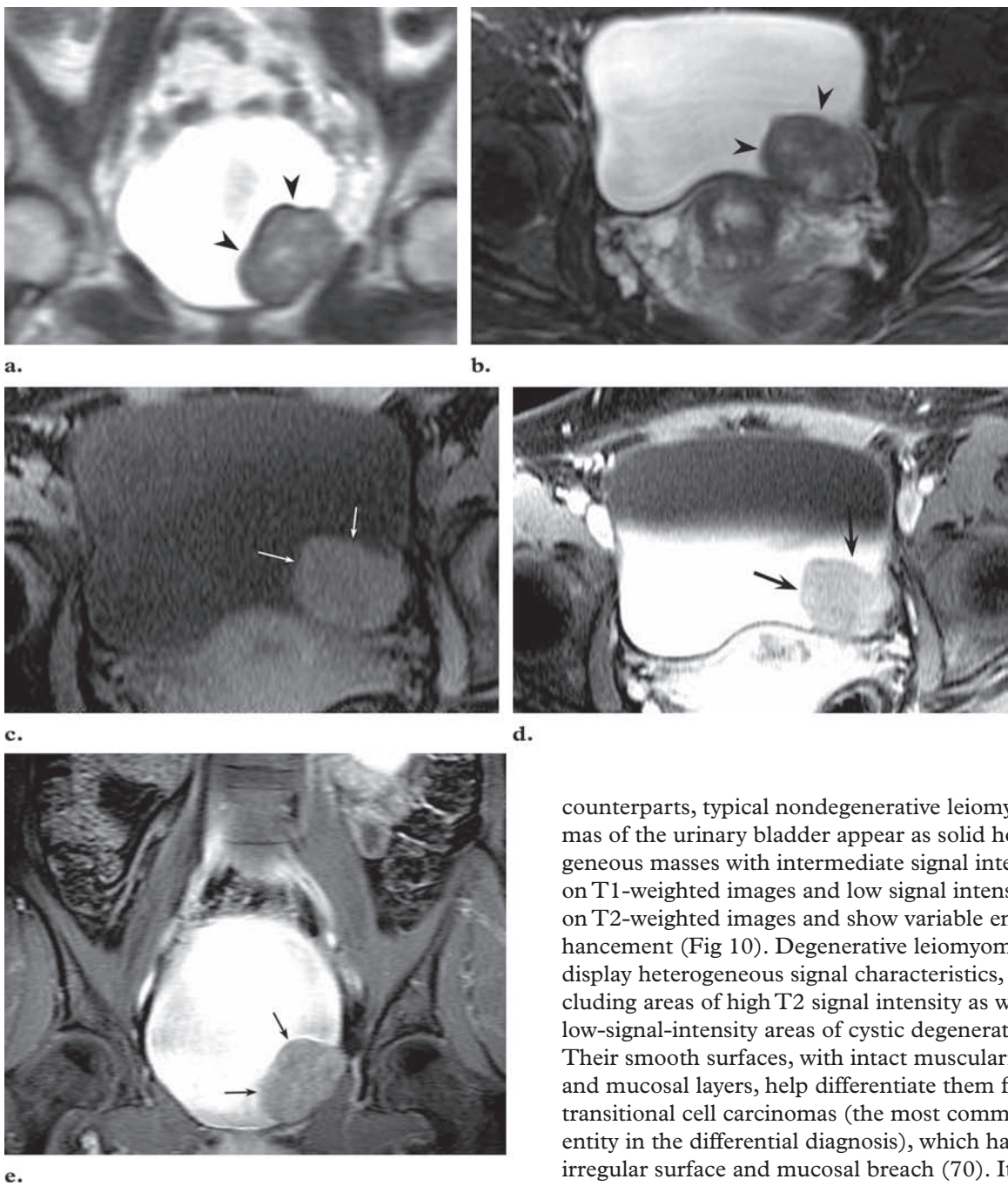


Figure 9. Urethral leiomyoma in a 46-year-old woman with symptoms of urinary frequency, urinary urgency, and dyspareunia. **(a)** Transabdominal US image shows a well-circumscribed relatively homogeneous mass at the level of the urinary bladder neck (arrows). **(b)** Transvaginal US image depicts the same well-defined mass (arrows) with a whorled internal appearance. **(c–e)** Axial **(c)**, sagittal **(d)**, and coronal **(e)** T2-weighted fast SE MR images obtained for further characterization show intermediate to low signal intensity in the mass (arrows in **c** and **e**, arrowheads in **d**), which is localized to the proximal urethra. At cystoscopy, narrowing of the proximal part of the urethra was found. The mass was surgically excised, and pathologic analysis of a specimen showed it to be a benign leiomyoma.

determine the symptoms, surgical approach, and prognosis. Common symptoms (occurring in 15%–20% of cases) are related to voiding; they include dysuria, frequency or hesitancy in urination, dribbling, and hematuria. Pedunculated intraluminal masses may lead to outflow obstruction (69). Lesions that develop outside the bladder lumen may remain asymptomatic for a long time and may be large when detected.

Pelvic US, CT, and MR imaging are helpful for assessing the site, dimensions, and morphologic features of the tumor. Although US may be useful in localizing intravesical and intramural

Figure 10. Leiomyoma of the bladder in a 45-year-old woman with urinary frequency and urgency. **(a, b)** Coronal non–fat-suppressed **(a)** and axial fat-suppressed **(b)** T2-weighted fast SE MR images show a well-circumscribed low-signal-intensity mass (arrowheads) along the left posterolateral aspect of the bladder. **(c)** Axial unenhanced T1-weighted fat-suppressed fast SE image shows that the lesion (arrows) has signal isointense to that of pelvic muscle, a finding suggestive of smooth muscle origin. **(d, e)** Axial **(d)** and coronal **(e)** contrast-enhanced T1-weighted fat-suppressed MR images depict homogeneous enhancement of the mass (arrows). The mass was surgically excised, and the bladder wall was repaired. Analysis of a specimen prepared with the frozen section technique helped confirm the diagnosis.



lesions, differentiation of an extravesical lesion from a pathologic entity in the adnexa may be challenging. MR imaging, with its superb contrast resolution and multiplanar capabilities, usually depicts features that are suggestive of the diagnosis, and these findings may help avoid unnecessary radical surgery. Like their uterine counterparts, typical nondegenerative leiomyomas of the urinary bladder appear as solid homogeneous masses with intermediate signal intensity on T1-weighted images and low signal intensity on T2-weighted images and show variable enhancement (Fig 10). Degenerative leiomyomas display heterogeneous signal characteristics, including areas of high T2 signal intensity as well as low-signal-intensity areas of cystic degeneration. Their smooth surfaces, with intact muscularis and mucosal layers, help differentiate them from transitional cell carcinomas (the most common entity in the differential diagnosis), which have an irregular surface and mucosal breach (70). It may not be possible to differentiate leiomyoma from leiomyosarcoma on the basis of imaging alone. However, leiomyosarcomas tend to be poorly defined and invasive, with marked heterogeneity on T2-weighted images and with nonenhancing areas secondary to necrosis observed on contrast-enhanced images (71).

Although an assessment with MR imaging may help increase the physician's confidence in the preoperative diagnosis of small tumors with typical imaging characteristics, cystoscopic biopsy and histopathologic analysis are required to verify the diagnosis. The selection of a management method is based on the symptoms, since the tumors typically have a benign course. Small tumors are treated with transurethral resection; larger tumors and those with extravesical components often require partial cystectomy. As is true of urethral leiomyomas, malignant transformation of urinary bladder leiomyomas has not been reported, and recurrence is uncommon (68).

Summary

Leiomyomas occur infrequently outside the uterus. Although they are histologically benign, extrauterine leiomyomas may mimic malignant tumors at imaging and may present a diagnostic challenge. The clinical symptoms and imaging features depend on the location of the lesion and on its growth pattern. A typical whorled appearance at US, and signal intensity similar to that of smooth muscle at T1- and T2-weighted MR imaging, strongly favor a diagnosis of leiomyoma. Familiarity with potential extrauterine sites and with the complete spectrum of imaging features characteristic of these tumors, including their more unusual manifestations, facilitates their timely diagnosis and appropriate management.

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RadioGraphics

Leiomyomas beyond the Uterus: Unusual Locations, Rare Manifestations

Najla Fasih, FRCR, et al

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Page 1932
Knowledge of the unusual and protean imaging manifestations of these almost always benign entities is essential to distinguish them from malignant tumors that may bear a close resemblance.

Page 1933
The most important entity in the differential diagnosis of diffuse peritoneal leiomyomatosis is peritoneal carcinomatosis, which typically manifests with weight loss, ascites, and disease progression observed at imaging.

Page 1934
The radiologic imaging appearance of pulmonary nodules in benign metastasizing leiomyomas varies from solitary subcentimetric lesions to multiple lesions mimicking pulmonary metastases from malignant tumors.

Page 1935
Intravenous leiomyomatosis-a rare disease that is histologically benign but clinically aggressive-is characterized by the intraluminal growth of leiomyomas in intrauterine and systemic veins. These lesions are implants from coexistent or previously resected uterine fibroids.

Page 1941
MR imaging is the most useful imaging modality for characterizing these tumors, because, regardless of their anatomic location, classic leiomyomas have signal intensity similar to that of smooth muscle on images obtained with any MR pulse sequence. However, histopathologic analysis is usually required to confirm the diagnosis.