Leiomyomatosis beyond the uterus: intravenous leiomyomatosis, disseminated peritoneal leiomyomatosis, retroperitoneal leiomyomatosis and benign metastasizing leiomyoma

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Learning objectives

Describe the uncommon growth patterns of extrauterine leiomyomas.

Summarize the clinical presentation, pathologic features, differential diagnosis and the management of these entities.

Highlight the spectrum of imaging findings that help guide the diagnosis and management of extrauterine leiomyomas with uncommon growth patterns.

Background

**INTRAVENOUS LEIOMYOMATOSIS (IVLM)**

- Rare entity first described in 1896 by Birch-Hirschfeld. In 1907 Durck reported the first case of IVLM with extension to the heart.

- Is characterized by the intraluminal growth of leiomyomas in intrauterine and systemic veins.

- IVLM is a very aggressive tumor, although histologically benign. The tumor usually enters through the lumen of the iliac vein and extends upward to varying locations, including the IVC, adrenal and renal veins, and right heart (intracardiac leiomyomatosis) Fig. 3 on page 9. Pulmonary artery extension occurs in 10% of cases Fig. 4 on page 10. Another route of tumor extension is via the ovarian vein (with subsequent spread to the renal vein and IVC). Local spread to bladder or retroperitoneal /parametrial space is less frequent.

- Anecdotic cases of IVLM coexisting with disseminated peritoneal leiomyomatosis are described in the literature.

Epidemiology

Most common in the fifth decade (ages ranging from 20 to 81 years). Most patients had undergone a previous hysterectomy/myomectomy or had a coexisting uterine leiomyoma.
Pathology and pathogenesis

- The pathogenesis of the tumor remains controversial, there are two main theories regarding its origin: intravenous extension of the uterine leiomyoma, or direct tumorigenesis from the wall of the venous system. Most cases have been associated with uterine leiomyoma.
- Macroscopically IVLM has a serpentine appearance, with a mean length of 31 cm.
- The tumor is confined to the vascular channels in contradistinction to benign metastasizing leiomyoma.

Clinical relevance

It is an insidious process that may lead to heart failure, pulmonary embolism, or even sudden cardiac death. It can be fatal due to extension of the tumor along the IVC in to the right heart with subsequent obstruction of the venous return to the heart.

Differential diagnoses


2. Leiomyosarcoma arising from the wall of IVC: the most important entity in the differential diagnosis. 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.

3. Bland thrombus: it is distinguishable from a leiomyoma by its lack of enhancement following the administration of intravenous contrast.

4. Malignant thrombus: formed by metastatic renal cell carcinoma (RCC) or hepatic tumors; is easily differentiated if the primary tumor is visible at imaging. RCC is the most common tumor that can extend into IVC and right heart.

5. Myxoma: in contrast to the right-sided location of IVLM, myxoma has a left-sided predominance. Most myxomas originate from the interatrial septum with a stalk and may attach to the walls of the cardiac chambers.
Treatment and prognosis

Total surgical resection is the best treatment and should be performed as soon as possible, considering the risk of sudden death caused by total outflow tract obstruction.

Surgery can be performed as a two-stage operation with separate resections of the intracardiac tumor and the abdominopelvic tumor, or as a one-stage operation with total resection of the entire tumor. Fig. 9 on page 11

The short and long-term outcome of complete removal is excellent, with no recurrence or postoperative death reported. Recurrence after incomplete removal was found in one third of cases.

DISSEMINATED PERITONEAL LEIOMYOMATOSIS (DPL)

- Rare entity first described by Wilson and Peale in 1952.
- It is characterized by multiple peritoneal smooth muscle nodules of varying sizes, with a greater concentration in the pelvis.
- Spectrum of appearances, sometimes presenting as tiny peritoneal nodules (classic presentation) mimicking peritoneal carcinomatosis or as bulky intra- or extraperitoneal masses resembling leiomyosarcoma.

Epidemiology

Typically occurs in premenopausal women or during pregnancy.

Pathology and pathogenesis

DPL likely is the result of multifocal metaplasia of the peritoneum, possibly secondary to hormonal stimulation. A subset of LPD may be secondary to transcoelomic dissemination of a primary uterine leiomyoma rather than de novo peritoneal metaplasia. In fact, treatment of uterine leiomyomas with laparoscopic myomectomy has been implicated in the subsequent development of DPL due to dissemination of the tumor cells along the laparoscopic tract.
Clinical relevance

It is usually discovered incidentally. Most patients are asymptomatic but clinical features such as abdominal and pelvic pain, rectal or vaginal bleeding and, more rarely, gastrointestinal disorders have been reported. Malignant transformation is rare and in a few cases, metastases have been found in the liver and lungs.

Differential diagnoses

1. Peritoneal carcinomatosis: is the most important entity in the differential diagnosis, which typically manifests with weight loss, ascites, and disease progression observed at imaging. By contrast, the absence of clinical symptoms and of a known primary malignancy, characterized by insidious, asymptomatic development is suggestive of a benign cause such as DPL.

2. Leiomyosarcoma

3. Endometriosis: DPL do not show the marked T1 hyperintensity that is seen in endometriosis.

4. Primary peritoneal 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.

5. Lymphoma: findings of predominant retroperitoneal lymphadenopathy and homogeneously attenuating, nonnecrotic, noncalcified lymph nodes favor a diagnosis of untreated lymphoma.

6. Tuberculosis: The fibrotic type of peritoneal tuberculosis usually can be differentiated by the observation of hypoattenuating features that are representative of associated necrotic mesenteric lymphadenopathy.

7. Desmoids tumors

Treatment and prognosis
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. Therefore, close surveillance is mandatory.

**Synonyms**

Diffuse peritoneal leiomyomatosis; leiomyomatosis peritonealis disseminata.

**RETROPERITONEAL LEIOMYOMATOSIS (RL)**

- Rare entity first described by Lewers in 1903.
- Retroperitoneal growth is another unusual growth pattern of leiomyomas.
- Multiple leiomyomatous masses are usually seen in the pelvic retroperitoneum and rarely may extend to the upper retroperitoneum, as high as the level of the renal hilum.

**Epidemiology**

RL is a rare neoplasm. Up to 40% of patients with RL have either a concurrent or a remote history of uterine leiomyoma.

**Pathology and pathogenesis**

It is unclear whether RL may originate from remnants of müllerian or wolffian ducts in the retroperitoneal space, from hormonally sensitive smooth muscle elements in the retroperitoneum, or as a result of metastasis from uterine leiomyoma.

**Clinical relevance**

RL may enlarge considerably yet remain asymptomatic and be detected incidentally at routine check-up or autopsy. Common symptoms of retroperitoneal leiomyomas include abdominal discomfort, fatigue, backache, dyspareunia, and urinary and bowel complaints.
Differential diagnoses

1. **Parasitic leiomyoma**: it is a distinct entity that arises when a leiomyoma becomes adherent to the retroperitoneal connective tissue, develops an auxillary blood supply, and loses its attachment with the uterus.

2. **Cervical leiomyoma**: occasionally may grow into the retroperitoneal space, simulating a primary pelvic retroperitoneal mass at imaging.

3. There is a broad spectrum of primary pelvic retroperitoneal masses in adults. It includes common benign and malignant neoplasms of neurogenic origin (schwannoma, paraganglioma, ganglioneuroma, extraadrenal pheochromocytoma) as well as teratoma, desmoid tumor, hemangioma, extra-adrenal angiomyelolipoma, sarcoma, lymphoma, and metastatic tumors. 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.

Treatment and prognosis

Surgical removal of the mass is the mainstay of treatment, which can be by laparotomy or laparoscopic removal. Abdominal hysterectomy along with the resection depends on the age of the patient, her symptomatology, and associated uterine leiomyoma. The prognosis of the patients with retroperitoneal leiomyoma is good.

**BENIGN METASTASIZING LEIOMYOMA (BML)**

- Rare entity first described by Steiner in 1939.
- Single or multiple morphologically benign smooth muscle tumors are found in extrauterine locations, especially the lungs, in women with a history of typical uterine leiomyomas. BML should only be diagnosed after a uterine or extrauterine leiomyosarcoma has been excluded.
BML seems to be a tumor with benign histology but with the biologic behavior of a malignant tumor.

Epidemiology

Typically occurs in premenopausal women. Almost all have had a history of uterine surgery for leiomyomas, on average 10 years before presentation.

Pathology and Pathogenesis

Metastases most often affect the lungs, whereas the heart, brain, lymph nodes, bone, and skin are more rarely affected.

Although some investigators consider BML as multifocal hyperplastic or neoplastic proliferations of smooth muscle in response to hormonal stimulation, there is increasing evidence that many are a result of vascular or lymphatic dissemination from uterine leiomyomas.

Clinical relevance

It is usually discovered incidentally on imaging performed for other reasons. Most patients with persistent disease have an indolent clinical course. Occasionally symptoms of chest pain, shortness of breath, and cough may be present. The tumors may continue to grow and result in respiratory failure and death. Spontaneous resolution of BML has been described.

Differential diagnosis

1. **Metastases from malignant tumors**: is the most common differential diagnosis. The majority of malignant lung metastases originate from breast, colorectal, prostate, bronchial, head-and-neck, and kidney cancers and all can mimic metastatic disease from uterine lesions.

2. **Uterine leiomyosarcoma with pulmonary metastasis**: the incidence of sarcomatous degeneration from a uterine leiomyoma is extremely rare, reported to be 0.1-0.8%.
Leiomyosarcoma usually presents as a massive uterine enlargement with irregular central zones of low attenuation, suggesting extensive necrosis and hemorrhagic. Foci of calcification may be present. The pattern of tumor spread is to the myometrium, pelvic blood vessels and lymphatics, contiguous pelvic structures, abdomen, and then distantly, most often to the lungs.

Treatment and prognosis

BML is slow-growing and hormone-sensitive. Bilateral oophorectomy should thus be considered in patients who still have unresected ovaries. If the patients are symptomatic, metastatic lesions should, whenever possible, be resected. If the tumors are not resectable, or if the patient refuses surgery, hormonal therapy may prevent further growth of the tumors.

Synonyms

Metastatic leiomyoma

Images for this section:
**Fig. 3:** Axial steady-state-free-precession (SSFP) MR images. Linear filling defect (arrow) in the right atrium (a), prolapsing across the tricuspid valve in the cine images (not shown). This defect extends into the pulmonary artery trunk (b).
**Fig. 4:** Axial contrast-enhanced CT image shows a filling defect in the right pulmonary artery (arrow). This finding was initially interpreted as pulmonary thromboembolism. The patient did not respond to anticoagulant drug therapy and the cordlike solid lesions were surgically excised. The diagnosis of IVLM was histologically proven.
**Fig. 9:** The patient underwent a two-stage operation with separate resections of the intracardiac and right pulmonary artery tumor in a first stage, and resection of the abdominopelvic tumor in a second stage. Surveillance MRI and CT examinations after surgery showed no recurrence of the disease. Axial contrast-enhanced CT image before surgery (a) shows widespread enhancing nodules (arrows) in the pelvis; after surgery (b) no recurrence is noted.
Fig. 10: 48-years-old woman with history of hysterectomy at age 38 due to uterine leiomyomas, presenting with low abdominal pain and urinary frequency. The physical examination revealed an abdomino-pelvic mass. A transvaginal ultrasound was performed, showing a large pelvic mass. Further characterization was obtained with an abdominopelvic MRI. Sagittal T2-W (a) and axial T1-W (b) images shows a huge abdomino-pelvic mass, that pushes the bladder anteriorly. No signs of invasion or of ascites were noted. The imaging findings could not reliably predict the retroperitoneal location of the mass, due to it large size, although the close location to the spine could suggest this location. Surgical excision helped confirm the retroperitoneal location.
**Fig. 12:** Axial T1-W fat-saturated pre (a) and post gadolinium (b) reveals predominantly homogeneous enhancement of the mass.
Fig. 11: (a) Coronal T2-W image shows a large polylobulated abdomino-pelvic mass with areas of increased signal intensity. (b) Coronal contrast-enhanced fat-saturated T1-W image shows predominantly homogeneous enhancement of the mass. The diagnosis of cellular leiomyoma was histologically proven.
Findings and procedure details

The superb contrast resolution and multiplanar capabilities of MR imaging make it particularly valuable for characterizing these tumors.

Multiplanar imaging (CT,MRI) depicts key anatomic points, such as ureter, bladder, or vessel involvement, that are crucial for surgical planning.

INTRAVENOUS LEIOMYOMATOSIS

- IVLM has some distinctive features on imaging, although the final diagnosis depends on histopathology. Fig. 5 on page 22

- CT and MRI are the most useful imaging modalities in the assessment of IVLM. Continuity of the intravascular tumor with the pelvic veins may be demonstrated. Fig. 1 on page 18 Fig. 2 on page 19

- Tumor extension is typically unilateral and occurs via two different routes, more commonly involving the uterine vein (with subsequent extension to the internal iliac vein, common iliac vein, and IVC) than the ovarian vein (with subsequent extension to the renal vein and IVC).

CT: typical findings consist of hypoattenuating intravascular filling defects and the associated uterine leiomyomas.

MRI: the intravascular tumor manifests as a mass of distended and folded tubular structures, described as having a solid "sausage-like" appearance. Relative to muscle, the tumor may be iso- to mildly hyperintense on T1-W images and mildly to markedly hyperintense on T2-W images, depending on the number of smooth muscle cells and fibrous tissue-containing hyalinized vessels the tumor contains. The tumor may demonstrate heterogeneous signal intensity due to the range of histologic appearances present within a single tumor, and may demonstrate homogeneous or heterogeneous enhancement following contrast material administration.
**Echocardiography**: typical features of intracardiac leiomyomatosis include an elongated mobile mass extending from the IVC into the right atrium and right ventricle, dilatation of the IVC and right cardiac chambers, and tricuspid regurgitation.

**US**: usually demonstrates vascularized thrombi within the pelvic veins and IVC.

An adequate preoperative diagnosis should provide detailed information about the tumor localization, extravascular and intravascular diameters, site of vascular entry, and patency of iliac and femoral veins. An adequate postoperative imaging follow-up is also important for recurrence detection.

**DISSEMINATED PERITONEAL LEIOMYOMATOSIS**

This entity reveals a spectrum of features ranging from multiple solid subcentimetric nodules like those in peritoneal carcinomatosis to large solid masses. Fig. 6 on page 23 Fig. 7 on page 24 The tiny peritoneal nodules of DPL may be below the resolution of all radiologic techniques. The masses may show homogeneous or heterogeneous attenuation with a variable enhancement pattern similar to that of uterine leiomyomas.

**MRI**: multiple masses with signal intensity similar to that of skeletal muscle and smooth muscle on both T1- and T2-W images and with homogeneous enhancement following the administration of contrast material. Fig. 8 on page 25

**18F-FDG PET/CT**: may be used to distinguish isometabolic activity of DPL from hypermetabolic uptake of leiomyosarcoma when peritoneal leiomyomatosis nodules are of sufficient size (6 mm or larger). However, malignancy can be definitively excluded only with histopathology.

**RETROPERITONEAL LEIOMYOMATOSIS**

The first step is to decide whether the tumor is located within the retroperitoneal space. It is useful to observe the displacement of normal anatomic structures. Anterior displacement of retroperitoneal organs (eg, kidneys, adrenal glands, ureters, ascending and descending colon, pancreas, portions of the duodenum) strongly suggests that the tumor arises in the retroperitoneum. Major vessels and some of their branches are also
found in the retroperitoneal space, so that displacement of these vessels can be helpful as well.

**CT**: RL appears as a well-defined homogeneous mass in the pelvic retroperitoneum. Calcification is rare.

**MRI**: RL demonstrates low T2 signal intensity, intermediate T1 signal intensity, and variable enhancement following contrast material administration. Primary retroperitoneal leiomyomas can be differentiated from retroperitoneal growth of cervical leiomyoma in that the latter usually shows contiguity with the cervix.

**US**: may depict a well-defined mass with a variable but usually homogeneous echotexture within the retroperitoneum. US-guided percutaneous biopsy of the mass is helpful for determining its histologic composition preoperatively.

**BENIGN METASTASIZING LEIOMYOMA**

The lung involvement in BML varies from solitary subcentimetric nodules to multiple nodules or masses. Cavitation of lesions occasionally takes place and rarely may be accompanied by pneumothorax. Calcification is rare. Occasional cases with a miliary pattern and a pattern simulating interstitial lung disease have been reported.

**CT** and **MRI**: both may be used to depict the pulmonary nodules in BML which have a nonspecific appearance and usually enhance homogeneously.

Although the multiplicity of lesions raises the question of metastatic disease, in the clinical setting of a hormonally active woman with a history of uterine leiomyomas and no known primary malignancy, the radiologist can add BML to the diagnostic considerations even before tissue sampling.

**Images for this section:**
**Fig. 1:** 76-year-old woman with history of hysterectomy at age 54 due to uterine leiomyomas. She presented with pelvic masses discovered during exploratory laparoscopy for acute episode of abdominal pain. CT and MRI imaging findings suggested extensive pelvic and intravenous leiomyomatosis with involvement of internal, external and common right iliac vein, IVC, right heart chambers, initial portion of the pulmonary artery trunk and right pulmonary artery. Coronal gadolinium-enhanced MR angiography images of the abdomen clearly depicted the cordlike tumor mass in the external iliac vein (open arrow) and IVC, extending to the right atrium (arrows). Enhancement of the tumor mass is fairly perceptible. Note the pelvic nodules (stars). There is a hepatobiliar cyst in the liver. RA - right atrium.
Fig. 2: Coronal (a) and sagittal (b) T1-W post-gadolinium fat-saturated fast SE MR images demonstrate right external iliac vein invasion (arrows) and a pelvic nodule (star).
Fig. 3: Axial steady-state-free-precession (SSFP) MR images. Linear filling defect (arrow) in the right atrium (a), prolapsing across the tricuspid valve in the cine images (not shown). This defect extends into the pulmonary artery trunk (b).
**Fig. 4:** Axial contrast-enhanced CT image shows a filling defect in the right pulmonary artery (arrow). This finding was initially interpreted as pulmonary thromboembolism. The patient did not respond to anticoagulant drug therapy and the cordlike solid lesions were surgically excised. The diagnosis of IVLM was histologically proven.
Leiomyomas with epithelioid cells with immunoreactivity for desmin (A-HE 400X; B-Desmin 400x).

**Fig. 5:** Histopathological examination of the tumor fragments surgically removed from right pulmonary artery, inferior vena cava and right internal iliac vein, confirmed the smooth muscle cell origin of the mass, consistent with the diagnosis of intravenous leiomyomatosis.
Fig. 6: 76-year-old woman with history of hysterectomy at age 54 due to uterine leiomyomas. She presented with pelvic masses discovered during exploratory laparoscopy for acute episode of abdominal pain. Transabdominal ultrasound image of pelvis demonstrates well-defined homogeneous isoechoic masses. No ascites was present.
Fig. 7: Axial contrast-enhanced CT image shows widespread enhancing nodules (arrows) in the pelvis but no evidence of ascites.
Fig. 8: Axial T1-W (a), axial T2-W (b) and sagittal T2-W (c) fast SE MR images shows several well-defined, round and fusiform pelvic nodules (arrows) with T1 hypointensity and T2 heterogeneous hyperintensity. Axial T1-W post-gadolinium fat-saturated (d) fast SE MR image depicts marked enhancement. This pattern is suggestive of leiomyomas with mixoid degeneration. B -bladder
Fig. 9: The patient underwent a two-stage operation with separate resections of the intracardiac and right pulmonary artery tumor in a first stage, and resection of the abdominopelvic tumor in a second stage. Surveillance MRI and CT examinations after surgery showed no recurrence of the disease. Axial contrast-enhanced CT image before surgery (a) shows widespread enhancing nodules (arrows) in the pelvis; after surgery (b) no recurrence is noted.
Fig. 10: 48-years-old woman with history of hysterectomy at age 38 due to uterine leiomyomas, presenting with low abdominal pain and urinary frequency. The physical examination revealed an abdomino-pelvic mass. A transvaginal ultrasound was performed, showing a large pelvic mass. Further characterization was obtained with an abdominopelvic MRI. Sagittal T2-W (a) and axial T1-W (b) images shows a huge abdomino-pelvic mass, that pushes the bladder anteriorly. No signs of invasion or of ascites were noted. The imaging findings could not reliably predict the retroperitoneal location of the mass, due to it large size, although the close location to the spine could suggest this location. Surgical excision helped confirm the retroperitoneal location.
Fig. 11: (a) Coronal T2-W image shows a large polylobulated abdomino-pelvic mass with areas of increased signal intensity. (b) Coronal contrast-enhanced fat-saturated T1-W image shows predominantly homogeneous enhancement of the mass. The diagnosis of cellular leiomyoma was histologically proven.
**Fig. 12:** Axial T1-W fat-saturated pre (a) and post gadolinium (b) reveals predominantly homogeneous enhancement of the mass.
Fig. 13: 48-years-old woman with history of hysterectomy at age 38 due to uterine leiomyomas. A large retroperitoneal abdominopelvic mass was surgically removed. Histopathological examination confirmed the smooth muscle cell origin of the mass consistent with diagnosis of leiomyoma.
Conclusion

Recognition of these entities can be challenging both clinically and radiologically, in part due to its rarity.

Their histologic features are essentially identical to benign uterine leiomyomas, but with quasi-malignant dissemination to the pelvic veins and vena cava, peritoneal cavity, or other distant sites, such as the lungs. Intracardiac extension of intravenous leiomyomatosis is potentially life threatening. The atypical location and aggressive growth of these tumors present a diagnostic dilemma and have led to controversy regarding their pathogenesis and actual "benignity".

IVLM should be suspected in middle-aged women with cardiac symptoms and a right atrial mass originating from IVC. IVLM is an underdiagnosed pathology and it is expectable an increased number of cases in the future.

Diagnosis of retroperitoneal leiomyomatosis is often challenging for radiologists and the first step is to decide whether the tumor is located within the retroperitoneal space.

Concerning to BML, although the multiplicity of lesions raises the question of metastatic disease, in the clinical setting of a hormonally active woman with a history of uterine leiomyomas and no known primary malignancy, the radiologist can add BML to the diagnostic considerations even before tissue sampling.

Radiologists aware of the key imaging features and the differential diagnosis to consider, in the appropriate clinical setting, can be the first to suggest the diagnosis of these intriguing entities.

Personal information

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