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REVIEW

MR Imaging of uterine sarcomas: a comprehensive review with radiologic-pathologic correlation

Filipa Alves e Sousa[1] · **Joana Ferreira**[2,3] · **Teresa Margarida Cunha**[4]

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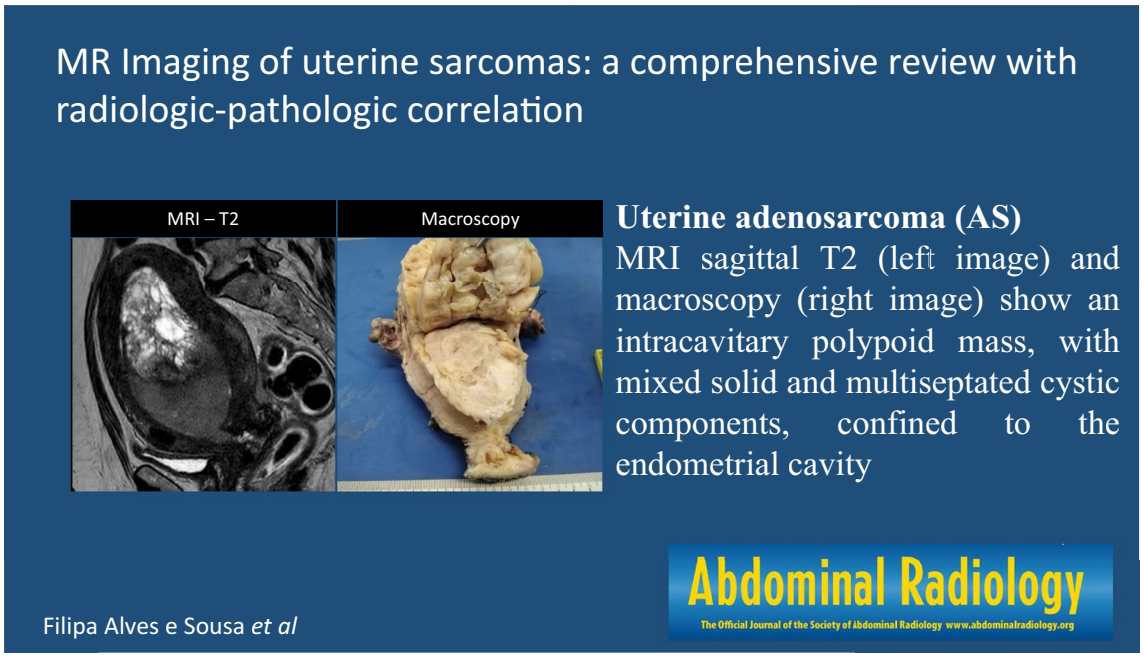
Abstract

The aim of this article is to summarize the MRI features of each sarcoma subtype and to correlate them with its pathological findings. Literature review through PubMed/Medline database to identify relevant articles on uterine sarcomas, with a special emphasis on their MRI findings and pathological features. While several, more generalistic, MRI findings of a uterine tumour should raise suspicion for malignancy (including irregular contour, intra-tumoral necrosis/hemorrhage and low ADC values), some particular features may suggest their specific histological subtype such as the gross lymphovascular invasion associated with endometrial stromal sarcomas, the "bag of worms" appearance of the low-grade endometrial stromal sarcoma and the "lattice-like" aspect of adenosarcomas which results from the mixed composition of solid and multiseptated cystic components. Knowledge of the different histological uterine sarcoma subtypes, their specific MRI features and comprehension of their pathological background allows for a more confident diagnosis and may indicate the correct histological subtype.

Graphic abstract



Keywords Uterine sarcoma · Leiomyosarcoma · Endometrial Stromal Sarcoma · Adenosarcoma

✉ Filipa Alves e Sousa
filipasousa039@gmail.com

Extended author information available on the last page of the article

Abbreviations

ADC	Apparent diffusion coefficient
AS	Adenosarcoma

ESS	Endometrial stromal sarcoma
CA125	Cancer antigen 125
CE-MRI	Contrast-enhanced magnetic resonance imaging
DWI	Diffusion-weighted imaging
HG-ESS	High-grade endometrial stromal sarcoma
HLRCC	Hereditary leiomyomatosis and renal cell carcinoma
LDH	Lactate dehydrogenase
LG-ESS	Low-grade endometrial stromal sarcoma
LM	Leiomyoma
LMS	Leiomyosarcoma
MRI	Magnetic resonance imaging
T2WI	T2-weighted imaging
SI	Signal intensity
UUS	Undifferentiated uterine sarcoma

Introduction

Uterine sarcomas comprise a heterogeneous group of rare uterine malignancies that arise from the myometrium or the connective tissue elements of the endometrium. They represent less than 10% of cancers of the uterine corpus and affect women of all ages with a higher incidence between 5th and 7th decades of life [1, 2].

They are the most aggressive type of uterine malignancies, displaying rapid growth and dissemination, and carrying a very poor prognosis with an overall 5-year survival rate ranging from 17.5% to 54.7% [3].

According to the 2020 World Health Organization (WHO) classification, the major histological subtypes are leiomyosarcoma (LMS), low-grade endometrial stromal sarcoma (LG-ESS), high-grade endometrial stromal sarcoma (HG-ESS), undifferentiated uterine sarcoma (UUS), and adenosarcoma (AS) [4].

Despite the intensive and ongoing search for more reliable diagnostic parameters, there are still no effective diagnostic criteria to determine the sarcomatous malignant nature of a uterine mass before surgery. Nevertheless, some MRI findings may raise suspicion for malignancy and even suggest the specific histological sarcoma subtype.

The final diagnosis is histological and usually requires large tumour sampling due to the often-large tumour dimensions and its heterogeneous composition, either by multisite biopsies or, preferably, by surgical resection.

This study aims to summarize the MRI features of each sarcoma subtype and to correlate them with its pathological findings.

Methods

The authors researched PubMed/Medline database to identify relevant articles on uterine sarcomas, with a special emphasis on their MRI findings and pathological features. Also, complementary insight from the author's personal experience is provided in some sections of the manuscript.

Clinical overview

Uterine sarcomas are rare, accounting for less than 10% of cancers of the uterine corpus, mostly occurring in patients over the age of 40 (mean age at diagnosis of approximately 60 years old), although they have been reported in patients as young as 20 years old [1, 2]. Black women have an approximately twofold higher incidence of leiomyosarcomas than white women (but not other types of uterine sarcoma) [5].

Some risk factors have been suggested, including exogenous hormone use, obesity, tamoxifen therapy, and prior pelvic irradiation, although some studies have not confirmed these associations [1, 6–9]. Women with Hereditary leiomyomatosis and renal cell carcinoma (HLRCC) syndrome have an increased risk for developing uterine sarcomas with an earlier onset of disease (13 to 17 years prior to their sporadic counterpart) [10]. Leiomyomas do not appear to be the precursor to leiomyosarcomas, with rare exceptions (atypical or cellular variants) [11].

Clinical presentation is nonspecific and includes pelvic mass, abdominal pain, and menstrual changes [12, 13]. Abnormal vaginal bleeding has shown higher sensitivity for the preoperative prediction of malignancy [14, 15]. Gastrointestinal or urinary tract symptoms may occur in the presence of regional tumour spread, and hemoperitoneum may follow tumour rupture. Nevertheless, most patients remain asymptomatic, further increasing the risk of misdiagnosing a leiomyosarcoma for a benign leiomyoma.

Biomarkers such as lactate dehydrogenase (LDH) and cancer antigen 125 (CA125) have low sensitivity as predictors for uterine sarcoma, but when elevated, may indicate advanced-stage disease [13].

The reported prevalence of unsuspected uterine sarcomas diagnosed after surgical resection is low (ranging from 0.2% to 0.4%), however, the consequences are devastating as some of the minimally invasive myomectomy techniques, often performed with morcellation, may inadvertently seed tumour cells throughout the abdomen causing iatrogenic metastatic disease [16].

While there is no validated screening process or international guidelines to reliably diagnose uterine sarcomas

preoperatively, the presence of clinical manifestations or a growing uterine nodule (presumed to be a myoma) in a postmenopausal woman who is not taking hormone replacement therapy, should raise suspicion for malignancy, in which cases further radiological evaluation may aid in making the correct diagnosis. Initial evaluation with ultrasound (preferably transvaginal ultrasound) may depict atypical findings for a benign myoma (including uterine mass with irregular/nodular contours, poorly defined margins, central necrosis, endocavitary location, extra-uterine invasion and/or the co-existence of enlarged pelvic lymph nodes or peritoneal metastasis) and prompt further investigation with pelvic MRI [17–19]. Nevertheless, uterine sarcomas depicted on MRI may be accidental and unsuspected.

The pre-operative histopathological diagnosis of uterine sarcomas by tumour biopsy has not gained widespread acceptance and this may be due to several reasons: large tumour dimensions and marked heterogeneity of its composition requires large sampling by multisite biopsies to avoid false-negative results, routine endometrial sampling will not provide a correct diagnosis for a myometrial-located tumour unless it has reached the surface of the endometrial cavity, and lastly the limited experience in transcervical needle biopsy and concerns about its risks and safety. Despite that, several studies [20–23] have shown that tumour biopsy (either by endometrial or transcervical approach) is a reliable and safe procedure for the differential diagnosis between uterine sarcoma and uterine leiomyoma, and should be encouraged as a diagnostic tool alongside pelvic MRI in patients suspected for uterine sarcoma. In two multicentre retrospective studies, uterine sarcomas were identified by endometrial sampling before surgery in 65% (74/114) [24] and 75% (36/48) [20] of cases.

Prognosis varies considerably according to the histological subtype, tumour stage, age, and tumour size, but in general they are characterized by their aggressive behavior and very poor prognosis with an overall 5-year survival rate ranging from 17.5% to 54.7% [3, 8, 17].

Uterine sarcomas are staged by the International Federation of Gynecology and Obstetrics (FIGO) staging system that was developed in 2009 and contemplates two different classifications systems: one for leiomyosarcomas and endometrial stromal sarcomas (Table 1) and another staging classification for adenosarcomas (Table 2). The differences in these staging systems account for their distinct biological behavior and tumour location since adenosarcomas tend to arise in the endometrium with subsequent invasion of the myometrium or cervical stroma in a similar fashion to endometrial carcinomas [25].

Standard treatment is total hysterectomy with bilateral salpingo-oophorectomy. Adjuvant treatment with chemotherapy and radiotherapy remains controversial, and is decided in a case-to-case basis [25].

General radiological considerations

Magnetic resonance imaging (MRI) is the imaging modality of choice to help in the differentiation of malignant uterine masses from benign tumours, as well as in the distinction of the different sarcoma subtypes and their local staging (assessment of local invasion, spread to adjacent organs and/or lymph nodes) [9, 12, 13, 26, 27].

The MRI protocol that we use at our institution includes: T1-weighted imaging (T1WI), T2-weighted imaging (T2WI) and Diffusion-weighted imaging (DWI) of the pelvis in the axial plane; T2WI in the axial, coronal and sagittal planes of the uterus; DWI in the axial plane of

Table 1 2009 FIGO Staging system for uterine leiomyosarcoma and endometrial stromal sarcoma

Uterine leiomyosarcoma and endometrial stromal sarcoma	
Stage I – Tumour limited to uterus	
IA	≤5 cm
IB	>5 cm
Stage II – Tumour extends beyond the uterus, within the pelvis	
IIA	Adnexal involvement
IIB	Involvement of other pelvic tissues
Stage III – Tumour invades abdominal tissues (not just protruding into the abdomen)	
IIIA	One site
IIIB	More than one site
IIIC	Metastasis to pelvic and/or para-aortic lymph nodes
Stage IV	
IVA	Tumour invades bladder and/or rectum
IVB	Distant metastasis

Table 2 2009 FIGO Staging system for uterine adenosarcoma

Uterine adenosarcoma	
Stage I – Tumour limited to uterus	
IA	Tumour limited to endometrium/endocervix with no myometrial invasion
IB	≤ 50% myometrial invasion
IC	> 50% myometrial invasion
Stage II – Tumour extends beyond the uterus, within the pelvis	
IIA	Adnexal involvement
IIB	Involvement of other pelvic tissues
Stage III – Tumour invades abdominal tissues (not just protruding into the abdomen)	
IIIA	One site
IIIB	More than one site
IIIC	Metastasis to pelvic and/or para-aortic lymph nodes
Stage IV	
IVA	Tumour invades bladder and/or rectum
IVB	Distant metastasis

the uterus; Dynamic contrast-enhanced (DCE) sequences in the most informative plane for the particular case being imaged for three scans to obtain arterial, portal and equilibrium phases with the last acquisition obtained in two orthogonal planes.

T2WI and DWI-MR should have the same acquisition plane, field of view, and slice thickness to allow side-by-side interpretation and/or image fusion as this improves diagnostic performance. T2WI sequences of the uterus may optionally be obtained with a reduced field-of-view (rFOV) as this increases spatial resolution and allows better anatomic detail. For the DCE-sequences we prefer to use 3-dimensional (3D) spoiled gradient-echo fat-suppressed T1-weighted imaging (3D T1WI FS) as it allows good spatial resolution with the possibility to reconstruct the acquired images in any desired plane. In cases where obstructive uropathy by tumour invasion/compression or upper abdominal tumour spread are suspected, we opt to include T2WI HASTE and DWI in the axial plane from the kidneys to the pelvis to assess for hydronefrosis, lymphadenopathy and/or peritoneal metastasis. Moreover, from our personal experience, we recommend fasting (4–6 h) and the administration of an anti-spasmodic agent prior to the examination (20 mg butyl scopolamine IM/IV or 1 mg of glucagon IV) unless their use is contraindicated due to patient medical background.

The complex histological composition of uterine sarcomas and the often present areas of tumour hemorrhage and/or necrosis account for the heterogeneous high to intermediate signal intensity (SI) on T2 weighted-imaging (T2WI) and the heterogeneous contrast-enhancement on contrast-enhanced MRI (CE-MRI). The high cellularity (characteristic of malignancy) accounts for the restricted diffusion that is depicted by high SI on diffusion-weighted imaging (DWI) with low signal intensity on the apparent diffusion coefficient (ADC) map [14].

MRI findings that favor the diagnosis of uterine sarcoma over a benign LM are the presence of necrosis (high T2 SI area with variable T1 SI and no enhancement on CE-MRI), hemorrhage (high T1 SI area with variable T2 SI and no enhancement on CE-MRI), irregular or nodular tumour margins (Fig. 1), endocavitary location, restricted diffusion with low ADC values, and finally, the co-existence of enlarged pelvic lymph nodes or peritoneal metastasis [14, 18, 28]. Nevertheless, no single criterion has been shown to accurately make the diagnosis of uterine sarcoma, and their diagnostic strength comes from the combined presence of multiple criteria.

General histological considerations

Uterine sarcomas may originate from myometrial smooth muscle cells (leiomyosarcoma [LMS]), from the endometrial stroma (endometrial stromal sarcoma [ESS] and undifferentiated uterine sarcoma [UUS]) or both (adenosarcoma[AS]) [4]. The UUS has been traditionally related to the ESS family of tumors but does not have a specific cell lineage and, therefore, it remains a diagnosis of exclusion. Adenosarcomas are mixed epithelial and mesenchymal neoplasms with a benign epithelial component and a malignant mesenchymal one. Other malignant mesenchymal tumors that may occur in the uterus are beyond the scope of this revision due to their extreme rarity. [4].

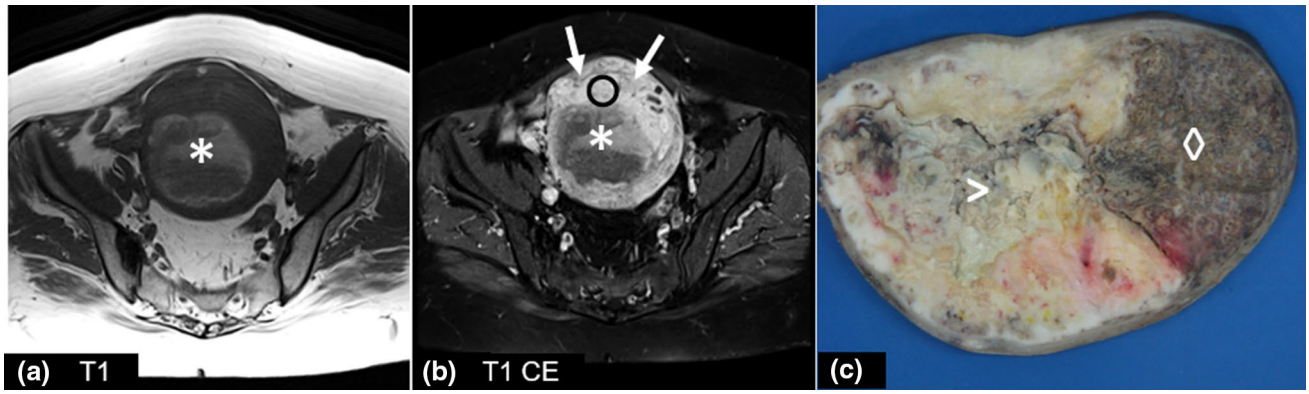


Fig. 1 Leiomyosarcoma in a 71-year-old woman. Axial T1-weighted image (**a**) and contrast-enhanced axial T1-weighted image with fat suppression (**b**) show uterine enlargement due to a heterogeneous myometrial tumor, with irregular border (→), and central hemorrhage and/or necrosis (*) depicted by central heterogenous hyperintensity on T1-weighted image that does not enhance after the administration of gadolinium. Note early intense enhancement in solid tumor components (Blck outline circle). Macroscopy of a leiomyosarcoma from another patient (**c**) demonstrates a large infiltrative tumor with areas of necrosis (>) and hemorrhage) (Black outline diamond)

Leiomyosarcoma

Uterine leiomyosarcoma (LMS) is a malignant mesenchymal tumour derived from myometrial smooth muscle cells, mostly arising de novo in the uterine corpus, and only in rare cases resulting from sarcomatous transformation of a pre-existing leiomyoma (0.2% of cases) [26].

Accounting for 40–50% of uterine sarcomas, LMS are the most common histologic subtype, with more recent studies showing a higher prevalence in the pre- and peri-menopausal women with an earlier age of onset (46–50 years, ranging from 32 to 71 years) than what was initially though as a post-menopausal disease with average age of onset > 50 years [16, 29, 30]. In about 33% of cases, patients present with distant metastasis, more frequently to the lungs [16]. Involvement of pelvic lymph nodes is uncommon and indicates advanced-disease [25]. Prognosis is poor even in early-stage disease with tumour confined to the uterus. The overall 5-year survival rate for all stages combined ranges from 15% to 25% [4].

Most uterine LMS manifest as a single and large myometrial intramural or subserosal nodule with necrosis and hemorrhage [4, 31, 32]. Three main histological subtypes are recognized: conventional/spindle cell, epithelioid and myxoid (Fig. 2), although mixed cell types are commonly present in the same tumor. Despite sharing the same diagnostic criteria (cytological atypia, tumor cell necrosis and mitotic count), the conventional/spindle cell subtype requires two of these criteria and a higher mitotic count (10 or more mitoses/10 high power fields) to establish the diagnosis, while fulfillment of only one criteria and a lower mitotic count are sufficient to make the diagnosis of the epithelioid or myxoid subtypes [4, 32]. Tumor cells express muscle markers such as desmin and h-caldesmon. Smooth muscle actin and positivity for CD10, EMA and cytokeratin are common [4]. All LMS should be considered as high-grade neoplasms [33].

Radiological findings of uterine LMS (Figs. 3, 4 and 5) overlap greatly with those of its benign, and much more common, counterpart leiomyoma (LM) – most typical distinguishing features are summarized in Table 3. Typical LM exhibits low T2 SI which would not be expected in a uterine sarcoma and does not pose a diagnostic challenge, however, up to 65% of LM show degenerative changes or are atypical LM (that is LM with unusual MRI features) which makes the differential diagnosis between some LM and uterine LMS very difficult [16, 28, 34, 35]. For instance, the high T2 SI depicted in uterine sarcomas can also be seen in atypical leiomyomas, cellular leiomyomas, and leiomyomas with cystic or myxoid degeneration; hyperintensity on DWI is seen in both cellular LM and uterine sarcomas due to their high cellularity; and intra-tumoral high SI areas on T1WI with fat suppression can either represent red degeneration from hemorrhagic infarction in a benign LM or tumour hemorrhage/necrosis which would make uterine sarcoma a more likely diagnosis [9, 14, 36, 37]. The ADC value has been given special attention in several studies that aimed to establish a cut-off value bellow which a tumour mass should be considered suspicious for sarcoma, with reported values ranging from 1.06×10^{-3} mm^2/sec to 1.23×10^{-3} mm^2/sec [9, 18, 38, 39]. A more recent study [28] advocates the use of a lower ADC cut-off value of 0.905×10^{-3} mm^2/sec to reduce the false-positive rate and also proposed a diagnostic algorithm, that reached a sensitivity of 98% and a specificity of 96%, which classifies uterine masses as highly suspicious for uterine sarcomas if they meet the following criteria: intermediate/high T2 SI, high SI on DWI (higher than the endometrium or lymph nodes) and ADC $\leq 0.905 \times 10^{-3}$ mm^2/sec.

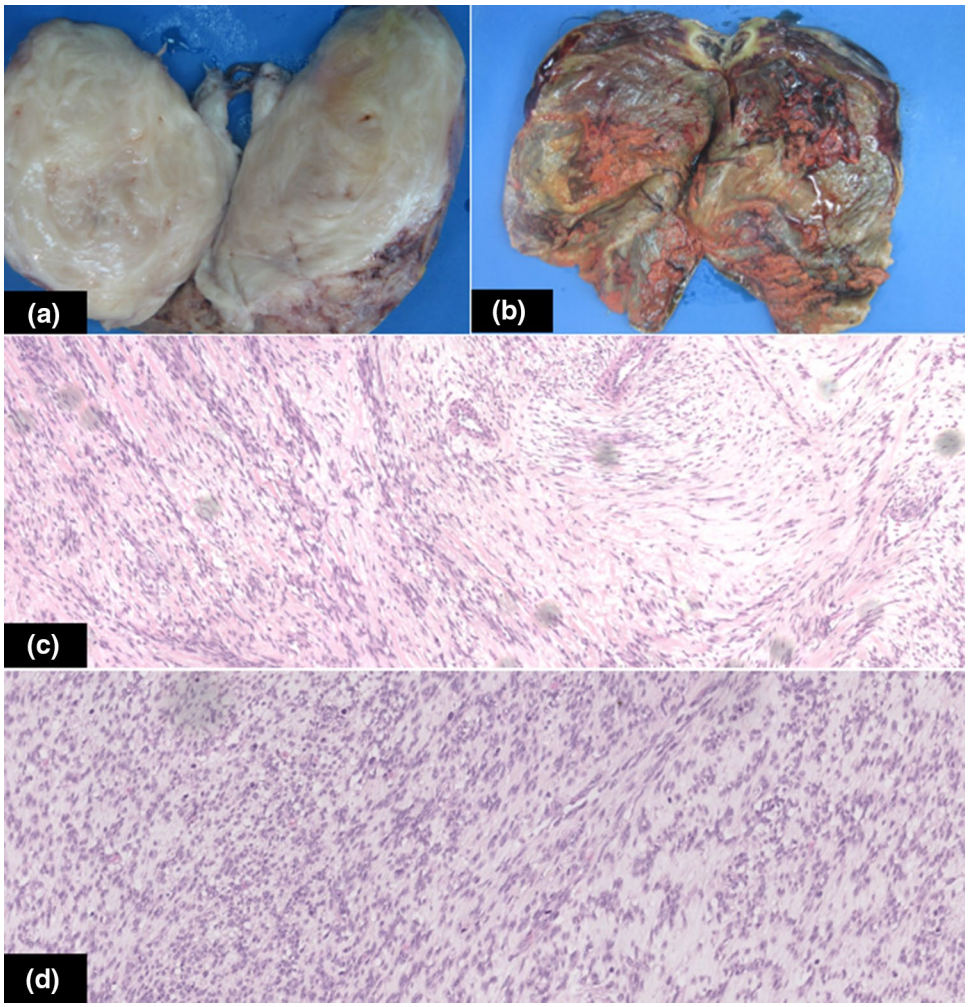


Fig. 2 Myxoid leiomyosarcoma in a 69-year-old woman. Macroscopically, a large, somewhat gelatinous, tumor (**a**) with hemorrhagic areas (**b**) can be observed. Histologically, a myxoid hypocellular foci next to conventional areas of leiomyosarcoma can be seen (**d**) as well as spindle cells with moderate cytological atypia and numerous mitoses (**c**)

Additionally, the most suggestive MRI findings of LMS are irregular contours, heterogeneous intermediate/high SI on T2WI, low ADC value and the presence of intratumoral necrosis (high T2 SI area with variable T1 SI and no enhancement on CE-MRI), hemorrhage (high T1 SI area with variable T2 SI and no enhancement on CE-MRI), cystic degeneration (high T2 SI with low T1 SI) and T2 "dark areas" (representing areas of previous hemorrhage that can be seen on T2WI as areas of signal intensity that are lower than that of muscles) [9, 14, 16, 18, 25, 26, 31, 40, 41]. A globally low T2 SI virtually excludes the diagnosis of LMS [28]. After the administration of intravenous contrast, LMS show avid enhancement, typically higher than other sarcoma subtypes [42, 43].

Endometrial stromal sarcomas

Endometrial stromal sarcomas (ESS) account for 10–15% of uterine sarcomas and encompass a subset of uterine malignancies of mesenchymal origin that is subdivided into low- and high-grade types [the former corresponding to low-grade endometrial stromal sarcoma (LG-ESS) and the latter including high-grade endometrial stromal sarcoma (HG-ESS) and undifferentiated uterine sarcoma (UUS)] [44].

LG-ESS tends to occur before menopause (mean age of 39 years old), it typically shows an indolent growth-pattern and is associated with a much better prognosis (5-year survival rate of 91%). On the other hand, HG-ESS predominantly affects slightly older women (mean age of 61 years old), and behaves more aggressively with rapid growth, extensive invasion and poor prognosis (5-year survival rate of only 33%) [45–47].

Negative prognostic factors implicated in LG-ESS include increased age and tumor size, whereas those implicated in HG-ESS include distant or nodal metastasis, omission of lymphadenectomy, and pathologically-positive surgical margins[45].

Surgery is the primary treatment for all ESS subtypes confined to the uterus, with additional adjuvant hormone therapy recommended for LG-ESS, and adjuvant systemic chemotherapy or radiotherapy for HG-ESS [45, 48].

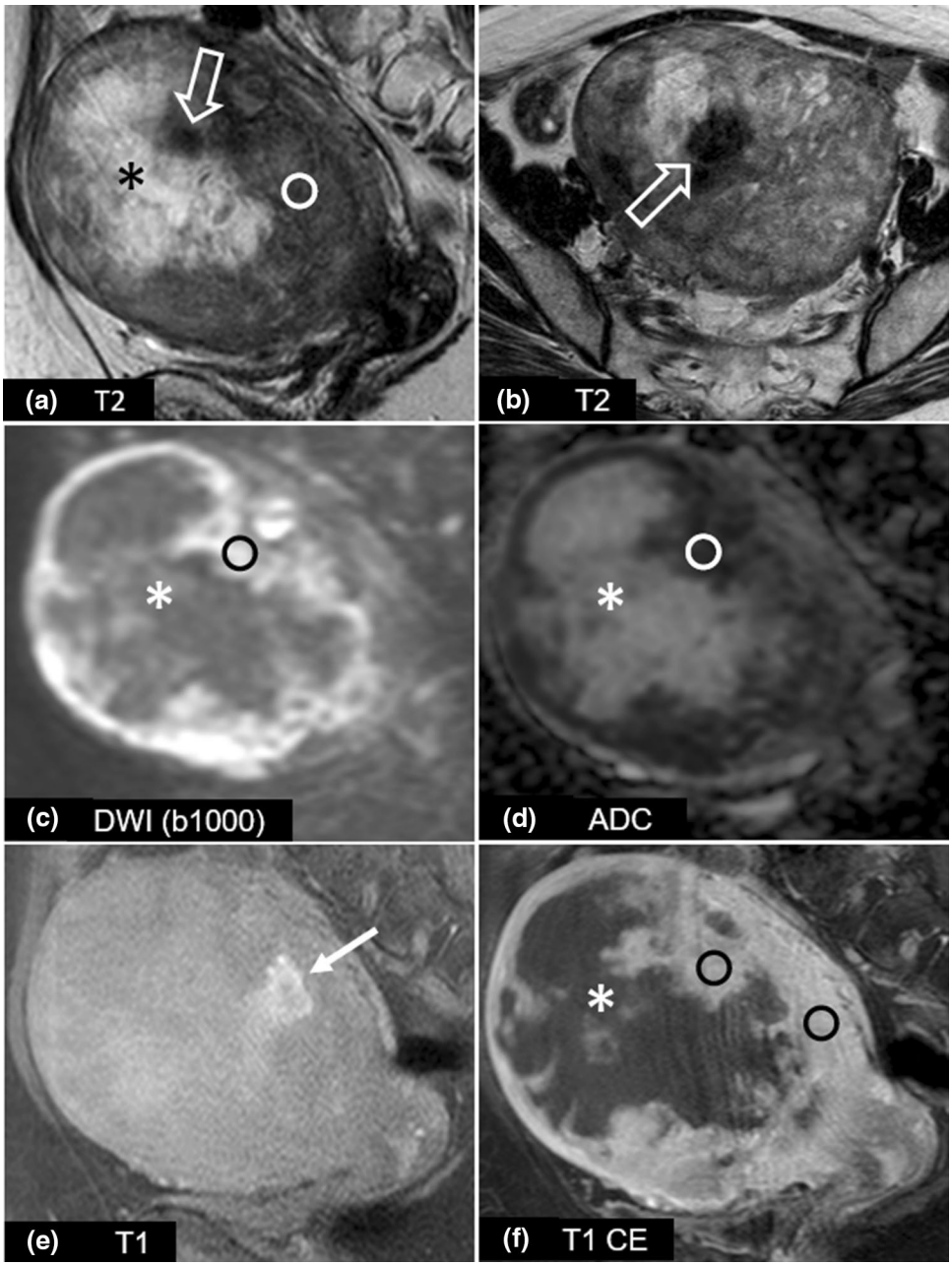


Fig. 3 Leiomyosarcoma in a 58-year-old woman. Sagittal (**a**) and axial (**b**) T2WI; sagittal DWI with b value = 1000 s/mm^2 (**c**) and ADC map (**d**); sagittal T1WI with fat suppression before (**e**) and after contrast administration (**f**) show: uterine enlargement due to a heterogeneous myometrial tumor displaying a heterogeneous solid component (Black outline circle) (depicted by intermediate signal-intensity on T2WI, restricted diffusion with high signal-intensity on DWI and low ADC values, and avid contrast-enhancement) and central necrosis (*) (depicted on T2WI as a heterogeneous central area of high signal intensity without restricted diffusion or contrast-enhancement), T2 "dark areas" (open arrow) and hemorrhage (→) (depicted on T1WI as a high signal intensity area)

Low-grade endometrial stromal sarcoma

LG-ESS display cells resembling proliferative-phase endometrial stroma, but in contrast to benign endometrial stromal nodules, this malignant entity demonstrates either myometrial invasion (3 or more foci of any depth or any foci ≥ 3 mm) or lymphovascular invasion [4, 49, 50]. Macroscopically, they are poorly defined, yellow to tan, intracavitary or intramural nodules (Fig. 6) [4, 49, 50]. Tumor cells express CD10, ER, PR and WT1, although smooth muscle actin and other muscle markers can also be positive. More than half (approximately 60%) contain the JAZF1/JJAZ1 translocation, although this translocation has also been found in endometrial stromal nodules [51]. Other common rearrangements include PHF1/JAZF1, EPC1/PHF1 and MEAF6_PHF1 [52].

LG-ESS are depicted at MRI by an often-large uterine mass of low T1 SI and heterogeneously moderate to high T2 SI, that grows as a polypoid endometrial tumour invading the myometrium, with either sharply demarcated margins or, more commonly, with diffusely infiltrative or nodular margins that are thought to reflect its growth-pattern along the adjacent lymphatics and vascular vessels. The latter form of tumor growth is more typical and usually results in preserved myometrial band-like areas of low T2 SI interspersed between the clusters of tumour cells in the myometrium,

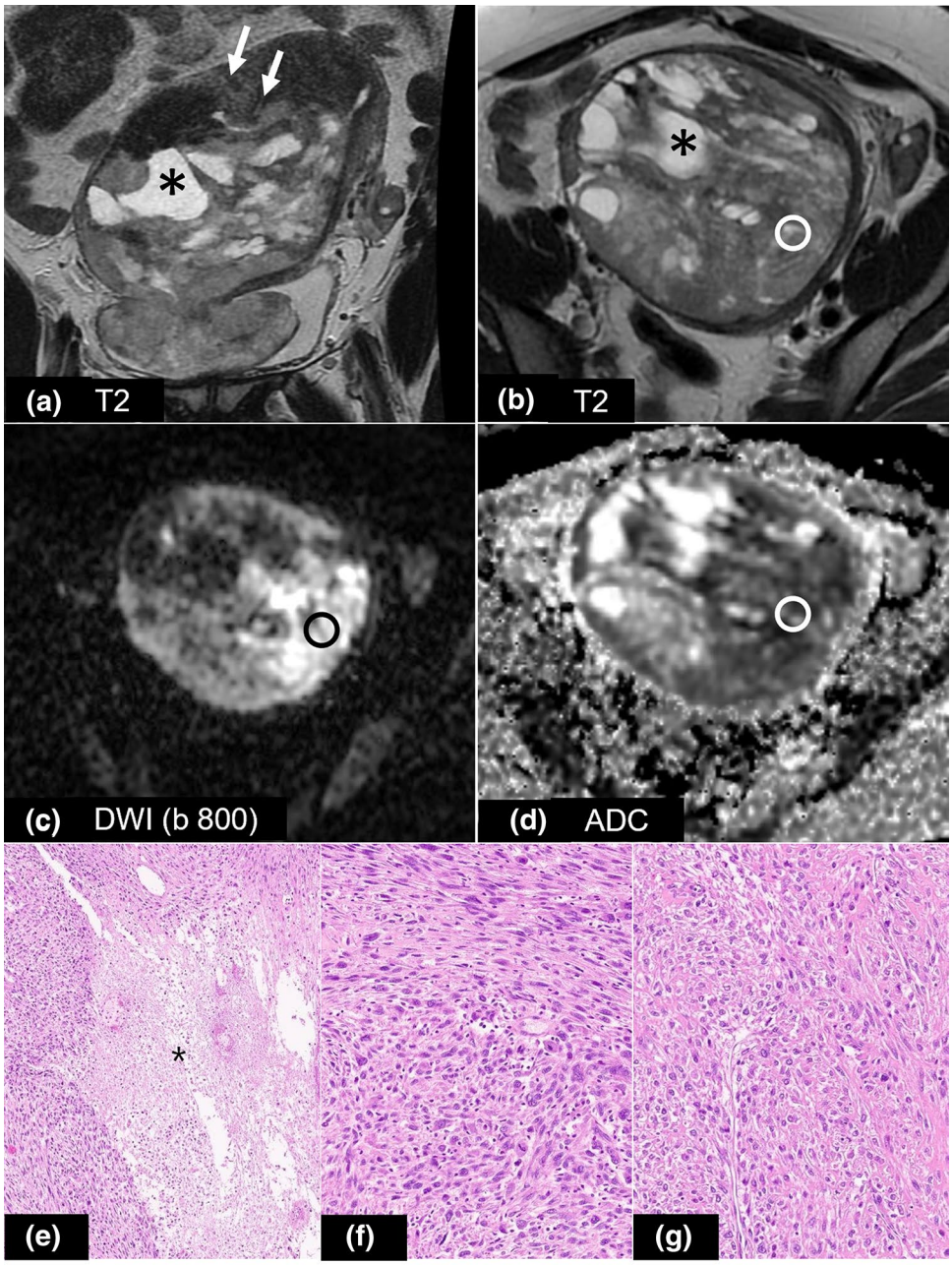


Fig. 4 Epithelioid leiomyosarcoma in a 42-year-old woman. Sagittal (**a**) and axial (**b**) T2WI; axial DWI with b value = 800 s/mm2 (**c**) and ADC map (**d**) show: uterine enlargement due to a heterogeneous myometrial tumor with irregular contour (→) displaying a heterogeneous solid component (Black outline circle) with high signal-intensity on T2WI and restricted diffusion [high signal-intensity on DWI and low ADC values]) and well as intra-tumoral cystic degeneration (*) (depicted on T2WI as homogeneous and well-limited areas of high signal intensity without restricted diffusion. Histologically, this tumor has foci of necrosis [(*) in **e**)] and shows cellular heterogeneity with some areas displaying neoplastic spindle-cells with severe cytological atypia (**f**), and other areas with a predominant epithelioid morphology (**g**)

giving rise to the "bag of worms" appearance that has been characteristically associated with this LG-ESS subtype, although it has also been described for HG-ESS (Fig. 7) [9, 26, 47, 53].

Less frequently, LG-ESS may arise in the stromal components of the myometrium with MRI features resembling those of a degenerated leiomyoma or even manifest as a diffuse heterogeneous myometrial thickening [25, 31]. Other reported MRI findings include a peripheral rim of low T2 SI, intra-tumoral areas of cystic degeneration (with high T2 SI and low T1 SI), and the co-existence of intra-myometrial nodules [47, 54].

Another interesting feature that may suggest the diagnosis of LG-ESS is the contiguous extra-uterine growth within the peri-uterine vessels, as well as along the uterine ligaments, fallopian tubes and ovaries (Fig. 8) [46]. This particular feature of gross intra-vascular extension is characteristic of this sarcoma subtype and accounts for its previous terminology – "Endolymphatic stromal myosis of the uterus". This appearance should be differentiated from the intravenous leiomyomatosis, a rare form of leiomyoma dissemination that may show similar findings but lacks features of tumour aggressiveness that would be expected in a uterine sarcoma such as irregular contour, intra-tumoral necrosis/

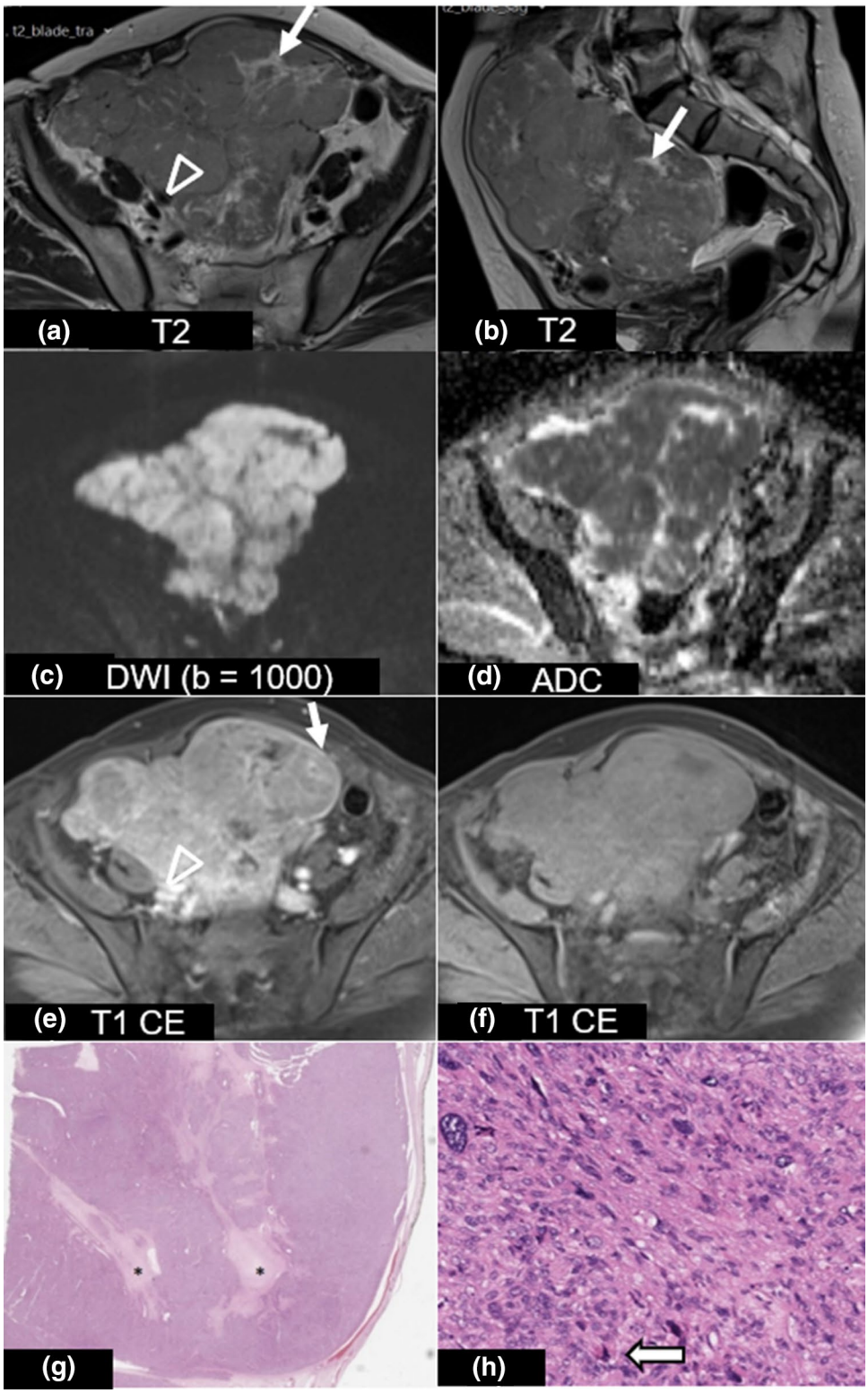


Fig. 5 Leiomyosarcoma in a 71-year-old woman. Axial (**a**) and sagittal (**b**) T2WI; axial DWI with b value = 1000 s/mm^2 (**c**) and ADC map (**d**); contrast-enhanced axial T1WI with fat suppression (**e** and **f**) show: large uterine tumor, with nodular borders, with intermediate signal intensity on T2WI, restricted diffusion (hyperintensity on DWI and low ADC values) and some intra-tumoral necrosis depicted on T2WI by high signal intensity areas (→) that do not enhance after the administration of gadolinium. Also note extensive extra-uterine tumor extension, with invasion of right adnexal area and right iliac vessels (Black outline triangle) confirming the aggressive tumor nature in keeping with malignancy. Histologically this is a multinodular tumour (**g**) with infiltrative areas and foci of necrosis (*) and it is composed of fascicles of spindle cells (**h**), some of which with severe cytological atypia (open arrow); numerous mitotic figures can be seen

Table 3 Distinguishing features between leiomyomas and leiomyosarcomas

	Typical features	Key points
LM	Multiple Low T2 SI Regular contours Confined to the uterus Low to high SI on DWI but lower than the endometrium or lymph nodes	✓ A globally low T2 SI virtually excludes LMS ✓ The combination of intermediate/high T2 SI, high SI on DWI (higher than the endometrium or lymph nodes) and ADC ≤ 0.905 × 10–3 mm2/sec is highly suspicious for LMS
LMS	Single and large Intermediate to high T2 SI T2 "dark areas" Irregular or nodular contours Extra-uterine invasion Areas of high T2 SI with no enhancement on CE sequences (likely representing tumour necrosis, haemorrhage, or cystic degeneration) High SI on DWI (higher than the endometrium or lymph nodes) Low ADC value (suggested cut-off values range from 0.905 to 1.23 × 10–3 mm2/sec) Enlarged pelvic lymph nodes or peritoneal metastasis	

ADC Apparent diffusion coefficient, *CE* Contrast enhanced, *DWI* Diffusion-weighted imaging, *LM* Leiomyoma, *LMS* Leiomyosarcoma, *SI* Signal intensity

hemorrhage, intermediate/high T2 SI, and restricted diffusion with low ADC values.

Tumour enhancement is commonly heterogeneous and iso- or hyperintense in comparison to the normal myometrium, this feature may be helpful in differentiating ESS from endometrial carcinoma which enhances less than the normal myometrium [25].

High-grade endometrial stromal sarcomas

Macroscopically, HG-ESS are usually seen as a large, intracavitary or intramural fleshy masses with hemorrhage and necrosis. Microscopically, they display monomorphic high-grade round and/or spindle cells and lymphovascular invasion, necrosis, and brisk mitotic activity, sometimes (in approximately 50% of cases) with an adjacent low-grade component [4, 55]. They harbor *YWHAE-NUTM2A/B* fusions (more commonly) but *ZC3H7B-BCOR* fusions, *BCOR* ITD and other rarer translocations have also been described [4, 56, 57]. Tumor cells typically express cyclin D1 and BCOR (more commonly expressed in those harboring YWHAE-NUTM2A/B fusion) [56, 58]. Due to their rarity, confirmatory genotype is desirable.

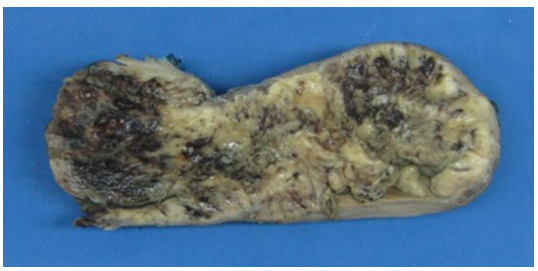


Fig. 6 Macroscopy of a low-grade endometrial stromal sarcoma seen as a large polypoid tumor infiltrating the myometrium and the cervix in a multinodular pattern

On MRI, similarly to LG-ESS, the HG-ESS also tends to present as a large and heterogeneous endometrial-based mass with intermediate to high T2 SI, with well-defined or infiltrative and nodular contour, and, less frequently, as a myometrial based tumor. Nevertheless, some findings may be more indicative of its higher-grade nature and may suggest the correct diagnosis. These include the larger areas of hemorrhage and necrosis, marked lymphovascular invasion, as well as a "feather-like" enhancement after the administration of intravenous contrast, which consists of a fine, wispy enhancement interspersed within tumors cells. This enhancement-pattern likely results from destructive myometrial invasion and was considered to be the most accurate diagnostic finding (95% of accuracy) in distinguishing high-grade from low-grade ESS in a retrospective study that compared MRI findings of 11 HG-ESS and 9 LG-ESS [53]. On T2-WI sequences, the hypointense preserved bundles of myometrial fibers are usually much thinner, scattered and harder to depict compared to low-grade lesions, due to a greater myometrial destruction (Fig. 9) [25].

Undifferentiated uterine sarcomas

Undifferentiated uterine sarcomas (USS) show no identifiable line of differentiation, rendering this a diagnosis of exclusion [4]. They are large intracavitary and polypoid or

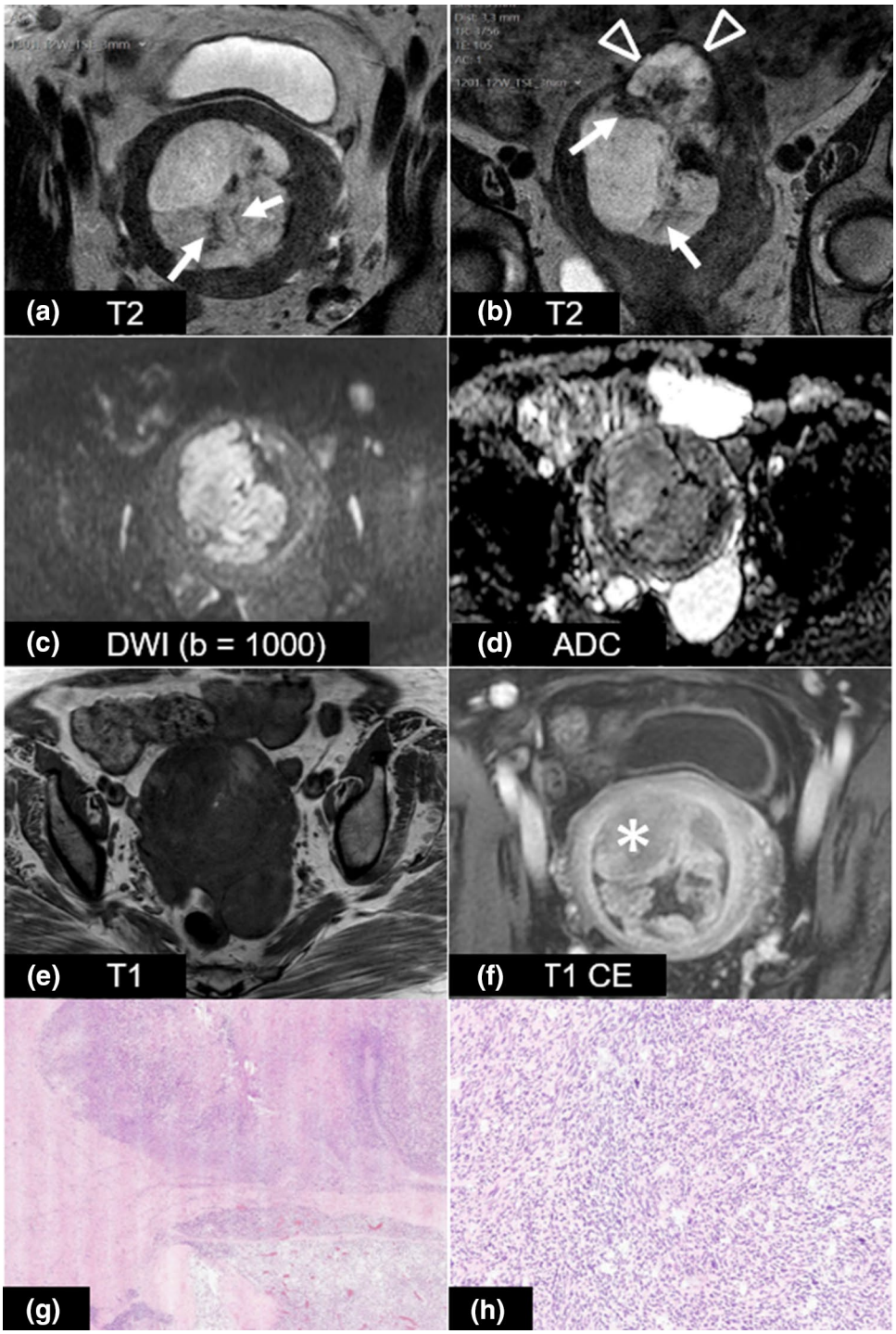


Fig. 7 Low-grade endometrial stromal sarcoma (LG-ESS) in a 64-year-old woman. Axial (**a**) and coronal (**b**) T2WI; axial DWI with b value = 1000 s/mm^2 (**c**) and ADC map (**d**); axial T1WI with fat suppression (*e*) and contrast-enhanced axial T1WI with fat suppression (**f**) show: intracavitary uterine tumor, with nodular borders, and myometrial invasion (Blck outline triangle), displaying high SI on T2WI, with intratumoral bands of low T2 SI (→) giving a "bag of worms" appearance, and restricted diffusion (hyperintensity on DWI and low ADC values). After the administration of contrast, tumour shows heterogeneous enhancement (*) that is isointense to the myometrium, a finding that helps in distinguishing it from endometrial carcinoma (which would enhance less than the myometrium). Histologic features include a multinodular tumor (**g**) composed of a uniform population of small blue cells reminiscent of proliferative phase endometrium (**h**)

intramural fleshy tumors with hemorrhage and necrosis and display uniform or pleomorphic high-grade mesenchymal cells with brisk mitotic activity. As this is a diagnosis of exclusion, exclusion of other high-grade tumors by extensive sampling, immunohistochemistry, and genotyping (in selected cases) is mandatory.

There are few studies describing the MRI features of USS, suggesting a lack of distinctive features and considerable similarity to HG-ESS, that is of a polypoid mass that frequently arises in the endometrial cavity with myometrial and lymphovascular invasion, with irregular margins, multiple marginal tumour nodules and extensive areas of haemorrhage and necrosis, with markedly heterogeneous enhancement (Fig. 10) [25, 59].

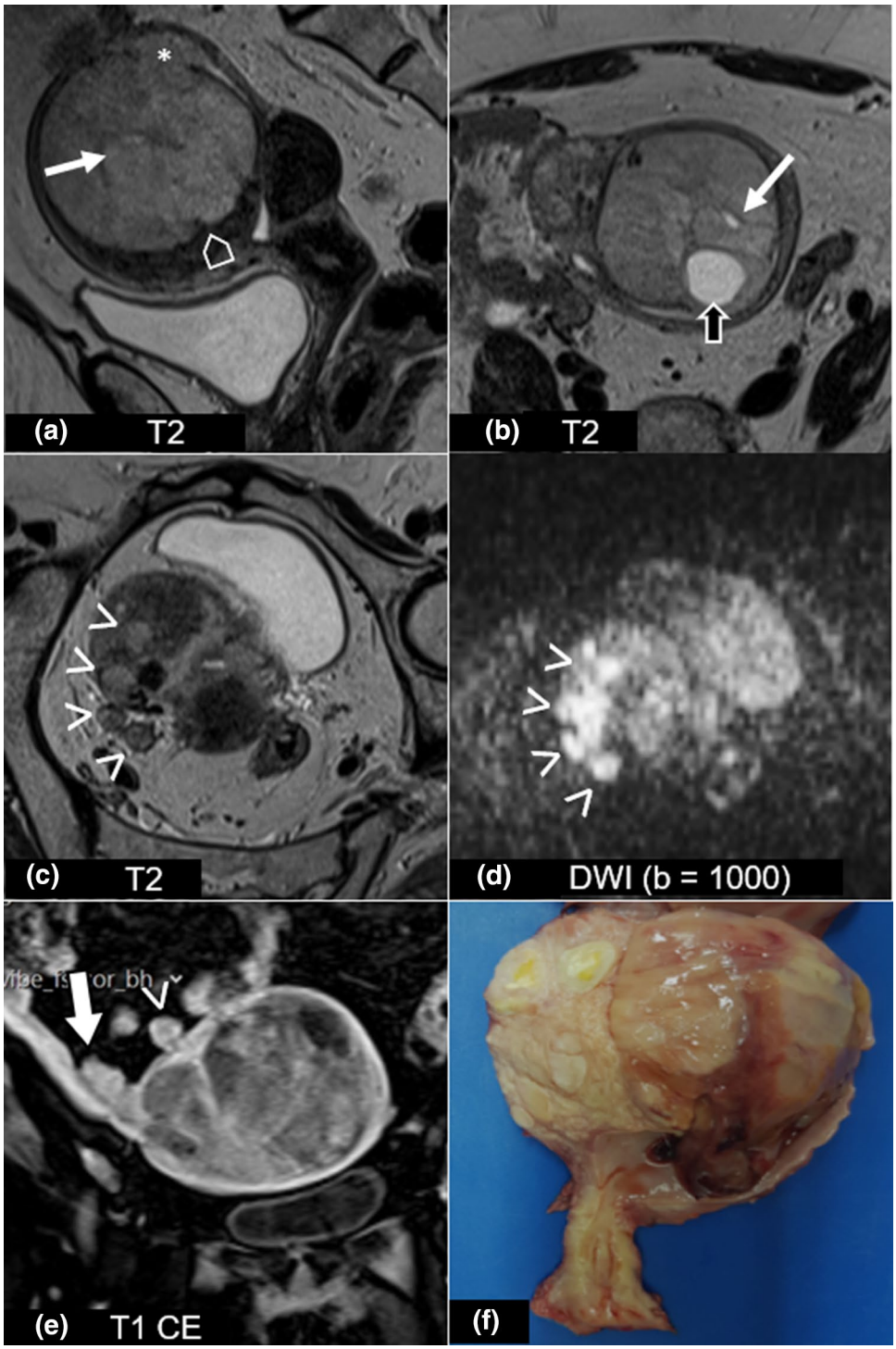


Fig. 8 Low-grade endometrial stromal sarcoma (LG-ESS) in a 73-year-old woman. Sagittal (**a**) and axial (**b**) T2WI show an intracavitary polypoid tumour with high T2 SI, cystic areas [black open arrow in (**b**)], irregular contours (⏢) and myometrial invasion (*) favouring the diagnosis of uterine sarcoma; also note intra-tumoral band-like areas of low T2 SI (→) giving rise to the "bag of worms" appearance which is typical of this sarcoma subtype; axial T2WI (**c**) and DWI with b value = 1000 s/mm^2 (**d**) at a different level depict gross nodular intra-vascular tumour extension (>); coronal contrast-enhanced T1WI with fat suppression (**e**) demonstrates contiguous extra-uterine growth within the peri-uterine vessels (>) and along the uterine ligaments (open arrow). Macroscopically (**f**), a polypoid intracavitary tumour with extensive myometrium infiltration can be seen

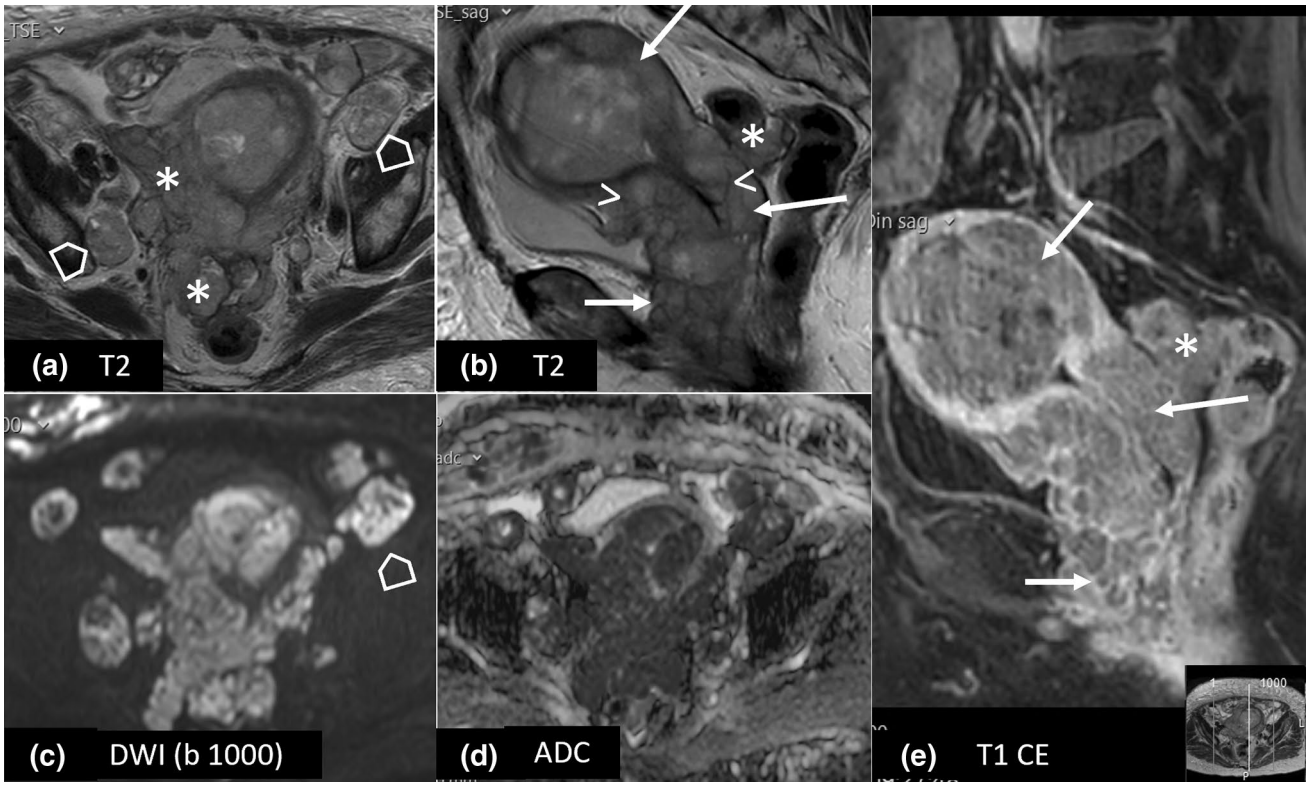


Fig. 9 High-grade endometrial stromal sarcoma (HG-ESS) in a 78-year-old woman presenting 8 years after cervical carcinoma of the uterus (IIB) treated with chemotherapy and radiation therapy. Axial (**a**) and sagittal (**b**) T2WI; axial DWI with b value = 1000 s/mm2 (**c**) and ADC map (**d**); sagittal contrast-enhanced T1WI with fat suppression (**e**) show a large uterine mass with an intracavitary component and extensive infiltration of the myometrium, cervix and vagina (→) with invasion of the parametria and mesorectum (*). Tumour demonstrates high SI on T2 WI sequences, with thin scattered bands of low T2 SI (>), restricted diffusion (with high SI on DWI and low ADC values), and heterogeneous contrast-enhancement. Also note bilateral external iliac lymph node metastasis (⌂)

Adenosarcomas

Uterine adenosarcomas (AS) are low-grade mixed epithelial and mesenchymal malignant neoplasms that account for 5–8% of cases of uterine sarcomas and less than 10% of uterine malignancies [60](WHO, AJCC). Macroscopically, they are usually solitary, exophytic and polypoid intracavitary masses that commonly prolapse through the cervical os. They are biphasic neoplasms composed of a benign epithelial component and a malignant stromal component forming leaf-like structures that resemble phyllodes tumors of the breast [61]. A more aggressive subtype where the sarcomatous component overgrowths the epithelial component – "adenosarcoma with sarcomatous overgrowth" – is acknowledged [62].

Considered to be a less aggressive sarcoma subtype that often presents at an early-stage, AS has a more favorable prognosis, with a 5-year survival of 79% in stage I disease [63]. The presence of sarcomatous overgrowth, myometrial invasion, lymphovascular space invasion and advanced stage have been associated with a worse prognosis [64]. Local recurrence of AS occurs in up to 30% of patients, mostly in the vagina [34].

On MRI, adenosarcoma are typically displayed by a large polypoid mass that distends the endometrial cavity, often protruding into the cervical canal, with well-circumscribed border and heterogeneous content, often demonstrating mixed cystic and solid components. Cystic areas are depicted by high T2 SI with low T1 SI and are typically multiseparated with lattice-like appearance (Fig. 11). The solid components may show scattered foci of high T2 SI, more likely to represent glandular epithelial components or necrosis [34, 65].

Interestingly, due to their low-grade nature, AS may be less restrictive to water diffusion, and show slightly higher ADC values in comparison to other uterine sarcoma subtypes [34, 46, 66]. AS enhancement after the administration of intravenous contrast is similar to that of the myometrium [9, 34] (Fig. 12). Myometrial invasion, intravascular or extra-uterine growth and distant metastases are consistent with sarcomatous overgrowth [26, 59].

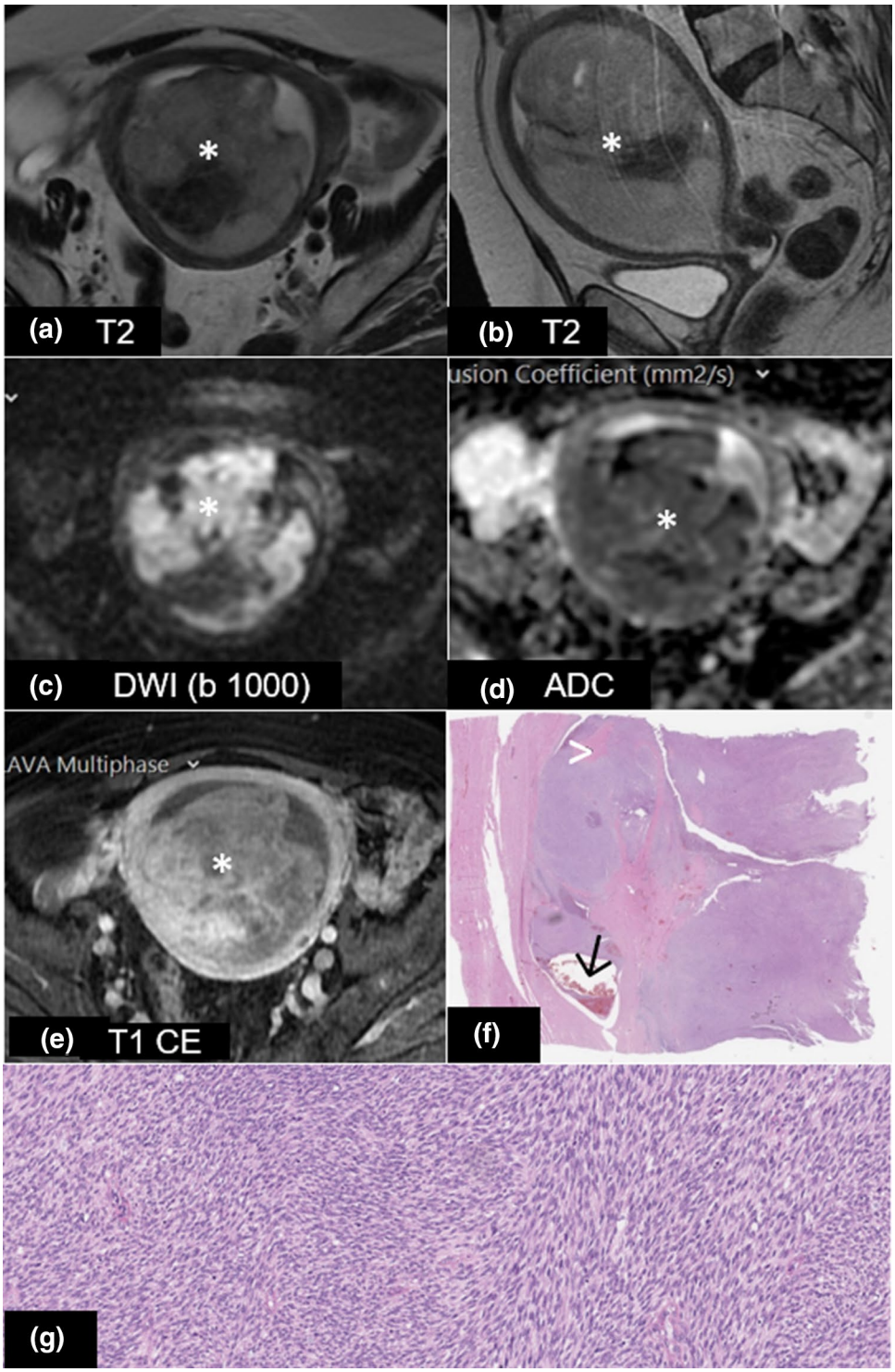


Fig. 10 Undifferentiated uterine sarcomas (USS) in a 79-year-old woman presenting with abnormal vaginal bleeding. Axial (**a**) and sagittal (**b**) T2WI; axial DWI with b value = 1000 s/mm^2 (**c**) and ADC map (**d**); axial contrast-enhanced T1WI with fat suppression (**e**) show uterine enlargement due to a large intracavitary polypoid mass (*) heterogeneously hyperintense on T2 WI sequences, with marked restriction to diffusion (high SI on DWI and very low ADC values), and heterogeneous contrast-enhancement isointense to that of the myometrium. Histologically, this is a vaguely nodular neoplasm that infiltrates the myometrium, with foci of necrosis (arrowhead) and hemorrhage (→) in (**f**). On lower power (**g**), short fascicles of monotonous spindle cells with numerous mitoses are observed

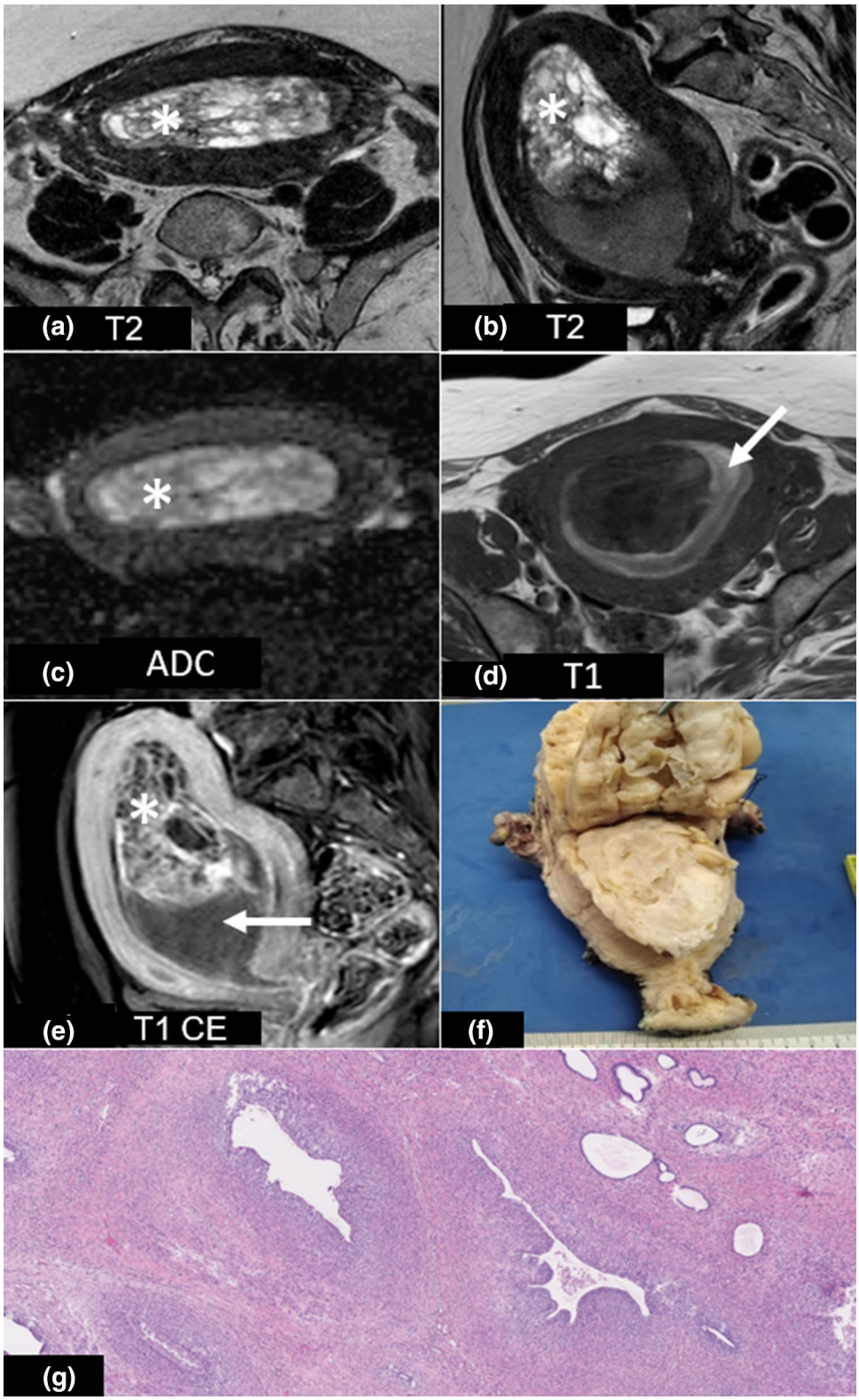


Fig. 11 Uterine adenosarcoma (AS) without myometrial invasion in a 66-year-old woman presenting with abnormal vaginal bleeding. Axial (**a**) and sagittal (**b**) T2WI show an intracavitary polypoid mass (*), with mixed solid and multiseptated cystic components giving a lattice-like appearance. On axial ADC map (**c**) tumour shows moderate restriction with ADC values slightly higher than those seen in other sarcoma subtypes; axial T1WI with fat suppression (**d**) depicts high-intensity fluid surrounding the tumour and filling the remaining endometrial cavity, that does not enhance in the sagittal contrast-enhanced T1WI with fat-suppression (**e**) in keeping with hemorrhagic content. Macroscopy (**f**) shows a partially cystic tumour confined to the endometrial cavity with a fleshy cut surface. Histologic features (**g**) include cysts and glands, some of which with a leaf-like architecture, surrounded by a thickened hypercellular stromal cuff

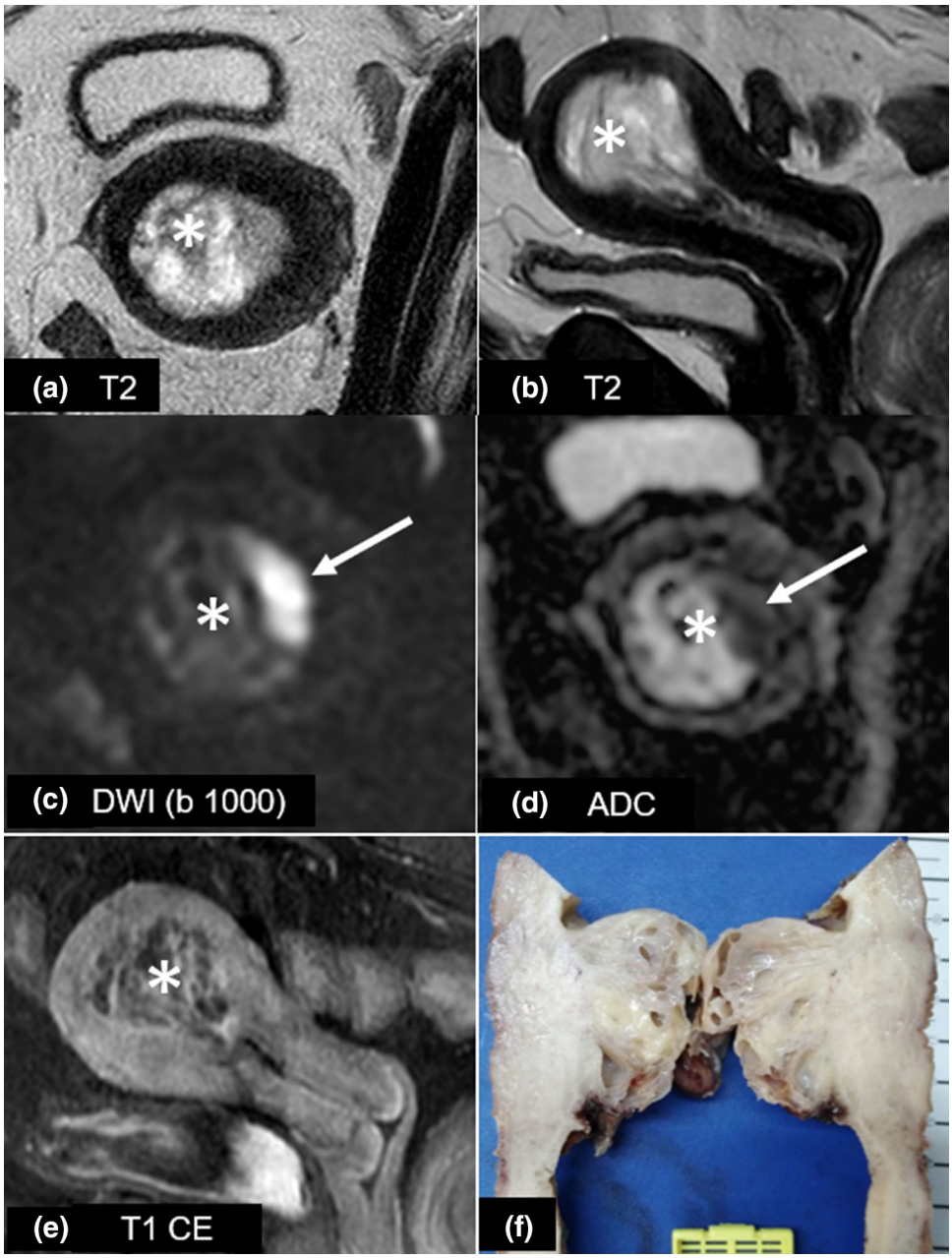


Fig. 12 Uterine adenosarcoma (AS). Axial (**a**) and sagittal (**b**) T2WI show an intracavitary polypoid mass (*), with mixed solid and multiseptated cystic components giving a lattice-like appearance. On axial DWI with b value = 1000 s/mm^2 (**c**) and ADC map (**d**) tumour shows an area of restricted diffusion (with high SI on DWI and low ADC values) (→); sagittal contrast-enhanced T1WI with fat-suppression (**e**) demonstrates heterogeneous enhancement. Macroscopically (**f**), a polypoid tumor with multiple cysts can be seen

Summary and key points

The most relevant and distinctive features of each uterine sarcoma subtype are summarized in Table 4.

The differential diagnosis between uterine sarcomas that arise in the endometrium and endometrial carcinomas may be challenging, especially for the less differentiated and more aggressive histologic type II endometrial carcinomas which encompasses grade 3 endometrioid tumors as well as tumors of nonendometrioid histology [67].

Compared to endometrial carcinoma, ESS usually shows larger dimensions, irregular and nodular margins, nodular extensions to the myometrium, and gross intra-vascular growth, which is not usually seen in endometrial carcinomas [68]. Adenosarcomas have a more distinctive T2 presentation due to their cystic components and lattice-like appearance. In contrast-enhanced sequences, endometrial carcinomas will enhance less than the myometrium as opposed to uterine sarcomas that are hypervascular in nature and are therefore iso- or hyperenhancing in comparison to the myometrium. Moreover, uterine sarcomas more frequently exhibit early peritoneal and haematogenous spread with distant metastases, in contrast to the regional lymph node spread typically seen in endometrial carcinomas [25].

Table 4 Summary of the most typical and discriminating features of each uterine sarcoma subtype

Histological subtypes	Typical features	Observations
LMS	Single and large myometrial based nodule Globally intermediate/high T2 SI Irregular or nodular contours Extra-uterine or endometrial invasion Areas of tumour necrosis, haemorrhage, or cystic degeneration	A globally low T2 SI virtually excludes LMS and favours the diagnosis of a benign leiomyoma The combination of intermediate/high T2 SI, high SI on DWI (higher than the endometrium or lymph nodes) and ADC $\leq 0.905 \times 10$–3 mm2/sec is highly suspicious for LMS over a leiomyoma
LG-ESS	Large polypoid endometrial mass with myometrial invasion (less frequently it may arise in the myometrium) Infiltrative or nodular contours (less frequently it may have a sharply demarcated contour) "Bag of worms" appearance Extra-uterine growth within peri-uterine vessels, uterine ligaments, fallopian tubes and ovaries	LG-ESS tends to occur in pre-menopausal women as opposed to HG-ESS that predominantly affects slightly older post-menopausal women Tumour enhancement on CE sequences is commonly iso/hyperintense in comparison to the normal myometrium as opposed to EC which enhances less than the normal myometrium
HG-ESS	Large polypoid endometrial mass with myometrial invasion (less frequently it may arise in the myometrium) Infiltrative or nodular contours (less frequently it may have a sharply demarcated contour) Larger areas of haemorrhage and necrosis "Feather-like" enhancement	On T2-WI sequences, the hypointense preserved bundles of myometrial fibers (that give rise to the "bag of worms" appearance in LG-ESS) are usually much thinner, scattered and harder to depict on HG-ESS
USS	Similar to HG-ESS without any distinctive feature	Considered a histological diagnosis of exclusion
AS	Large polypoid endometrial mass that commonly prolapses through the cervical os Well-defined contour Heterogeneous composition with mixed cystic and solid components "Lattice-like" appearance	Less restrictive to diffusion (higher ADC values) than other uterine sarcoma subtypes – may help in the differentiation from LG-ESS Shows iso-enhancement to the myometrium in CE sequences – may help in the differentiation from EC which is hypoenhancing

ADC Apparent Diffusion Coefficient, *AS* Adenosarcoma, *CE* Contrast-enhanced, *DWI* Diffusion-weighted Imaging, *EC* Endometrial Carcinoma, *HG-ESS* High-grade Endometrial Stromal Sarcoma, *LG-ESS* Low-grade Endometrial Stromal Sarcoma, *LM* Leiomyoma, *LMS* Leiomyosarcoma, *SI* Signal intensity, *USS* Undifferentiated Uterine Sarcoma

Conclusion

MRI findings of uterine sarcomas overlap greatly with those of benign (and more common) entities such as uterine leiomyomas, nevertheless, some radiological features should raise suspicion for malignancy. Knowledge of the different histological subtypes of uterine sarcomas and their specific MRI features allows for a more confident diagnosis and may indicate the correct histological subtype.

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Declarations

Conflict of interest The authors declare that they have no conflict of interest.

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Authors and Affiliations

Filipa Alves e Sousa[1] · Joana Ferreira[2,3] · Teresa Margarida Cunha[4]

[1] Department of Radiology, Centro Hospitalar Universitário de Lisboa Central, Alameda Santo António dos Capuchos, 1169-050 Lisbon, Portugal

[2] Department of Pathology, Instituto Português de Oncologia de Lisboa Francisco Gentil, R. Prof. Lima Basto, 1099-023 Lisbon, Portugal

[3] Nova Medical School, Universidade Nova de Lisboa, Lisbon, Portugal

[4] Department of Radiology, Instituto Português de Oncologia de Lisboa Francisco Gentil, R. Prof. Lima Basto, 1099-023 Lisbon, Portugal