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Ultrasound imaging of uterine leiomyomas and leiomyosarcomas – is there a reliable method to distinguish malignant and benign masses?

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ABSTRACT

Uterine myometrial tumors are predominantly benign conditions that affect one-third of women and represent the main indication for hysterectomy. Preoperative imaging is of utmost importance for characterization and for precise mapping of myometrial tumors to best guide therapeutic strategy. New minimally invasive therapeutic strategies including morcellation, myolysis, uterine artery embolization and image-guided radiofrequency or high-intensity focused ultrasound fibroid ablation have been developed for the treatment of women with symptomatic uterine leiomyomas. However, preoperative differentiation between atypical leiomyomas and leiomyosarcomas is critical on imaging as uterine sarcoma requires a specific surgical technique to prevent dissemination. A single, rapidly growing uterine tumor, associated with endometrial thickening and ascites, in post-menopausal women is suspicious of uterine endometrial stromal sarcoma and carcinosarcoma. Suggestive sonographic and MRI imaging features have been described, but overlap in imaging appearance between uterine leiomyosarcomas and cellular leiomyomas makes it challenging to ascertain the diagnosis. This review aims to illustrate the imaging features of atypical uterine fibroids, uterine sarcomas and their potential mimickers to make the reader more familiar with this serious gynecologic condition that needs special consideration.

Keywords: smooth muscle neoplasms, uterine fibroids, uterine sarcoma, ultrasound imaging, pattern recognition, STUMP, smooth muscle tumor of unknown malignant potential

INTRODUCTION

Leiomyomas (LM) are the most common estrogen-dependent uterine tumors that occur in 50–60% of women, rising to almost 70% by the age of 50 (Stewart, 2015; Wise, 2016). Even when asymptomatic, they may lead to infertility or they may present non-specific symptoms such as uterine bleeding, dysmenorrhea, dyspareunia and/or chronic pelvic pain (Freytag, 2021). These symptoms frequently reduce severely the life quality of affected women and their families. However, when patients with fibroids present with symptoms, it is not always possible to prove that they are actually caused by these particular type of uterine lesions (Donnez, 2016). On palpation and at surgery they frequently cause the uterus to appear bulky and may change the normal uterine contour (Fig. 1).

When symptomatic, these masses may represent indications for laparoscopic surgery and/or hysterectomy (Donnez, 2018). However, although vast proportion of all women in reproductive age may have uterine leiomyomas, only 10% of them has to be operated due to large tumor size or presenting symptoms. Some uterine fibroids have the capability to survive in the unfavorable conditions, having better adhesion ability, higher proliferation rate, and being more resistant to apoptosis (Raga, 2016). Intramural fibroids are usually well demarcated due to the formation of a pseudocapsule related to the compression of the surrounding myometrium. When the growth of these masses involves another outer or inner uterine myometrial layer, such fibroids are usually classified as subserous or submucous leiomyoma. Large uterine fibroids often degenerate as they outgrow their blood supply. The various types of degeneration include: (1) hyaline, (2) cystic, (3) myxoid, and (4) red degeneration. The most common, hyaline degeneration affects >60% of cases. In these masses tumor smooth muscle cells are replaced by proteinaceous tissue. Proliferation of myocytes and production of an extracellular collagenous matrix are two characteristic histological features found in

most leiomyomas. The collagenous matrix is often abundant in larger masses. In the areas in which the accumulating collagen is excessive, the myocytes are progressively separated from their blood supply, resulting in myocyte atrophy and eventually cell death. Hypocellular, hyalinized areas may be accompanied by cystic degeneration characterized by edematous and acellular tumor center while in hyaline degeneration (Flake, 2013). Two other rare types of degeneration are characterized by soft mucoid areas in myxoid type and tissue necrosis in red type fibroid. Rare leiomyomas manifestations and atypical site tumors include: metastasizing leiomyoma, peritoneal disseminated leiomyomatosis, intravenous leiomyomatosis, parasitic or retroperitoneal growth (Liu, 2021). Nevertheless, since the development of various types of uterine fibroids appears to be multifactorial with genetic and epigenetic factors controlling the progress of the disease, the etiology of these rare lesions remains unclear (Lagana, 2017; Ciebiera, 2020).

A large variation in fibroid growth rates has been described in the medical literature. Generally, these lesions may grow at very different rates and, conversely, they may even spontaneously regress (Li, 2021). The ability to predict the growth rate of fibroids with the use of various imaging techniques could help clinicians decide which their patients should be advised for treatment. For example, asymptomatic women with fibroids detected incidentally may require follow up if these lesions are likely to have a slow growth rate. Alternatively, surgical removal could be indicated in women with fast growing tumors. Vascularization type of fibroids is known to be important factor in tumor growth prediction. Abundant vascularity indicates growth potential and non-invasive treatments like e.g. high-intensity focused ultrasound (HIFU) or uterine arteries embolization are less effective in avascular fibroids (Łoziński, 2021; Pelage, 2005).

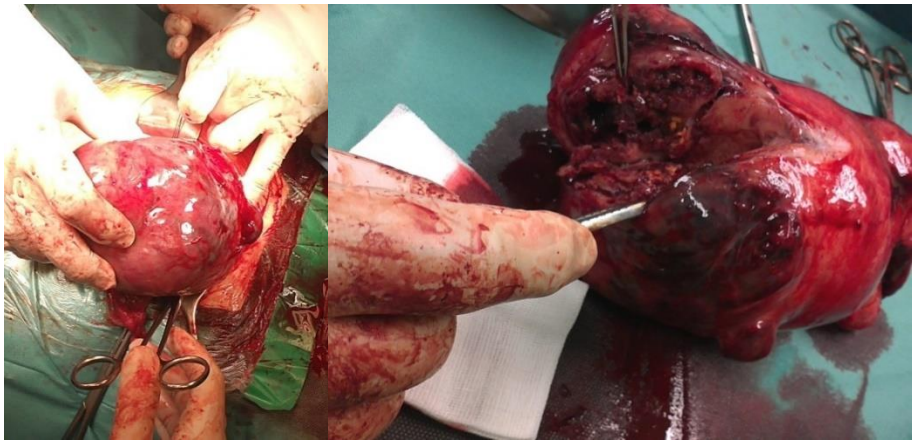

Figure 1. Typical macroscopic appearance of uterine leiomyoma at open surgery (A) and excised fibroid internal structure (B)

Rapid leiomyoma's growth, caused by its transformation into leiomyosarcoma (LMS) is rare and takes place in about 0.1-0.8% of all cases (Schwartz, 2006; Al Ansari, 2013; Bharambe, 2014). Preoperative identification of atypical uterine fibroids and sarcomas may be extremely difficult and time-consuming. In affected women a late diagnosis is a major problem and may contribute to disease progression and a worse response to surgical treatment. Currently most small and mid-sized uterine tumors can be removed with the use of minimally invasive laparoscopic surgery. Medical concerns indicated the increased longer-term morbidity associated with laparotomy and classical hysterectomy. When ovaries are removed there is an increased delayed pelvic bones fracture risk, cardiovascular disease, dementia, and pelvic floor prolapse. These possible complications have driven exploration of non-hysterectomy treatments for symptomatic uterine fibroids. In recent years several less invasive methods have gained an increasing role for this reason. These include fibroid morcellation at laparoscopic surgery, uterine artery embolization with polyvinyl alcohol derivatives, radiofrequency myolysis guided by transvaginal ultrasound, or HIFU under magnetic resonance imaging (MRI-HIFU)-guidance that destroys fibroid tissues (Donnez, 2016; Donnez, 2017; Laughlin-Tommaso, 2016). All these less invasive or non-invasive modalities are contraindicated in women with suspected malignant uterine lesions in order to avoid intra-abdominal tumor dissemination.

Uterine leiomyosarcoma accounts for 3-7% of all primary uterine malignancies with an incidence of 0.7 per 100,000 women (Rey Valzacchi, 2020). In a 10-years series of 921 hysterectomies or myomectomies for presumed myomas, Mühlenbrock et al. have found that the incidence of LMS was 1 in 460 (Muhlenbrock, 2021). In their group the incidence of any unexpected pathology in presumed myomas was 1 in 83 and included six atypical myomas, one leiomyoblastoma, one epithelioid myoma, two LMS, one mixed epithelial and mesenchymal tumor and one incidental cervical cancer. An important question can be asked here, if these malignancies could be suspected before surgery. Typically, solid uterine masses that at sonography demonstrate smooth and sharp margins, are homogeneous on gray-scale imaging and have peripheral concentric vascularity on color Doppler, in general are incompatible with the diagnosis of leiomyosarcoma. Since the risk of malignancy is low in these cases they are potentially suitable for minimally invasive treatments. On the other hand, some uterine leiomyomas may present atypical features that overlap with leiomyosarcomas, especially in younger females. Such "atypical" fibroids create the most difficulties in triaging patients to non-hysterectomy treatments. In clinical practice tumors derived from uterine smooth muscle cells present a broad spectrum ranging from leiomyosarcomas to leiomyomas, can be distinguished based on histopathological features including the degree of cytologic atypia, mitotic count activity (mitotic index per 10 high-power fields, HPFs), and presence of tumor cell necrosis.

However, in some of such lesions, these histopathological features may appear in an unusual combination which does not meet the diagnostic criteria of a leiomyoma or leiomyosarcoma. Such a heterogeneous group of lesions is characterized by histological and biological diversity that at histology cannot be certainly recognized as either a benign leiomyoma or a malignant leiomyosarcoma (Ip, 2009). These diagnostically challenging uterine solid masses are called "smooth muscle tumors of uncertain malignant potential" (STUMPs). Due to relative rarity of STUMPs their clinical behavior and prognosis have not been fully understood, yet, and the actual incidence of these tumors is still unknown. Moreover, even following detailed histological analysis a postoperative diagnosis of STUMP is also difficult due to the lack of uniform diagnostic criteria (Rizzo, 2020). Histologically, STUMPs are characterized by the proliferation of muscle cells in varying proportions and are classified into three categories according to the degree of differentiation: well-differentiated, intermediate-differentiated and undifferentiated. STUMPs are highly variable in size and may be as small as 2 cm and as large as 35 cm. The lesions are most often unilateral-98% of cases-solid or cystic-solid with smooth external surface. A capsular rupture is encountered in about 10% of cases, and ruptures are sometimes accompanied by ascites. Since the rate of extrauterine, intra-abdominal recurrence for atypical leiomyoma is low (<2%), the related risk for distant metastasis is a negligible (Rizzo, 2020). However, since the final histological diagnosis may be difficult, all women with confirmed STUMPs, especially when only myomectomy was performed should be informed of recurrence risk and monitored closely (Zhang, 2021).

In clinical setting, imaging techniques are crucial for the planning of medical or surgical treatment in women with gynecologic tumors. Pelvic ultrasound can be used both as primary or an adjunct modality to magnetic resonance imaging (MRI) of uterine lesions. Currently, computed tomography (CT) scan is not the investigation of choice for the characterization of pelvic masses. However, uterine fibroids are often seen incidentally on CT lower abdomen and pelvic scans performed for other reasons. The typical finding is a bulky, irregular uterus or a mass in continuity with the uterus. Ultrasound imaging in typical cases is capable to differentiate between LM and LMS and thus can help in planning treatment. However, there are also considerable limitations to the clinical application of selected ultrasound features that distinguish LM from LMS. Moreover, due to multiple differences in the ultrasound scanning techniques and parameters assessed by various studies and to the relative rarity of LMS at single institutions, there is continuing uncertainty regarding how to use and how to integrate various sonographic parameters with clinical and other imaging studies data to improve diagnostic accuracy. Typical problems with pelvic imaging of uterine smooth muscle tumors include:

1. the presence of multiple uterine masses in a single patient where

direct pathologic–imaging correlation may be difficult
2. variability of the imaging features of various fibroids in one patient that may lead to potential bias in reported results
3. assessement of echostructure within a hete-rogeneous mass, when this measure is non-standardized across various ultrasound systems
4. lack of blinded comparison of imaging characteristics and small numbers of fibroids and leiomyosarcoma cases and/or lack of measurement of interobserver agreement related to the imaging features that distinguish LM and LMS

This review aims to illustrate the ultrasound imaging features of typical and atypical uterine fibroids, sarcomas and other potential mimickers to make the sonographers more familiar with the preoperative differentiation between benign and malignant uterine smooth muscle cell tumors.

ULTRASOUND FEATURES OF LEIOMYOMAS

Two-dimensional (2D) gray-scale sonography is the primary imaging modality used to evaluate uterine fibroids. Preoperative ultrasound assessment of myometrial lesions is best performed by ultrasound experts, who compared with gynecologists, show a greater degree of agreement with histopathology and greater interobserver reproducibility of the imaging results. However, the experts in gynecological ultrasound are not always available and in clinical reality a standard sonographic examination is typically performed by non-expert examiners. In large uterine masses the difficulties of this imaging procedure may differ greatly due to the diverse clinical scenarios that include the echo distribution, placement depth, and number of fibroids found. The vast majority of uterine fibroids appear as oval or round isoechoic or hypoechoic, well-delineated single or multiple lesions located within the myometrium. However, various sonographic patterns have been described to date and the differences are thought to be due to the different forms of internal degeneration. Hypoechoic or anechoic spaces indicate the presence of areas of hemorrhagic and/or cystic degeneration or proteolytic liquefaction. A hyperechoic peripheral rim associated with posterior shadowing or a hyperechoic, internally speckled pattern is typical for a calcified uterine fibroid (Fig. 2.)

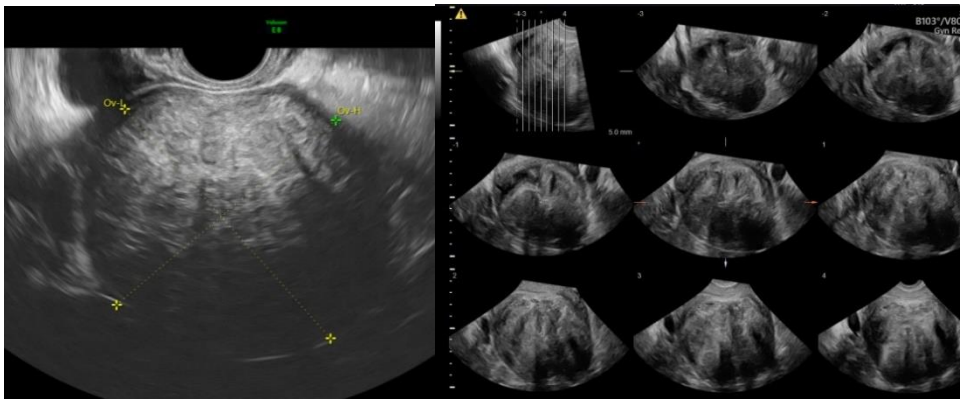

Figure 2. Transvaginal imaging of a typical, oval-shaped uterine leiomyoma with mixed echogenicity and posterior shadowing seen on 2D gray scale (A) and at tomographic three-dimensional ultrasound imaging (TUI)-image (B)

At ultrasound examination it may be clinically important to distinguish uterine fibroids and uterine adenomyosis. Adenomyosis usually appears enlarged, globular, with regular external contour, while fibroids not only cause the organ enlargement but also alter uterine contour (Cotrino, 2020). Typical sonographic features of adenomyosis include an inhomogeneous tissue with irregular and no defined borders that cause asymmetric thickening of the affected myometrium. The echostructure of adenomyosis is usually characterized by vascular spaces and radial stripes that, when moving the probe, may determine a visual effect called "rain in the forest sign" (Cotrino, 2020). Conversely, uterine fibroids appear as solid and well-defined lesions with a visible pseudocapsule and shadowing (Fig. 2A and 2B). Internal vascularity of typical uterine fibroids seen on color Doppler imaging is usually scant and typically peripheral (Fig. 3A and 3B).

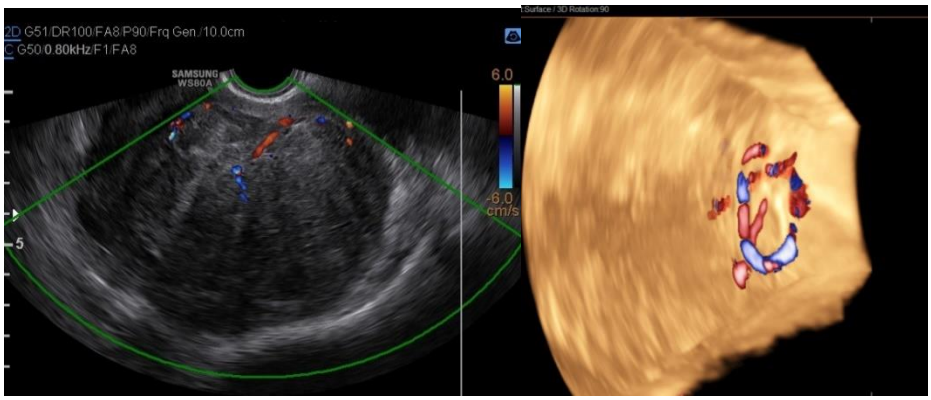

Figure 3. Transvaginal imaging of an oval-shaped uterine leiomyoma with mixed echogenicity and scant peripheral vascularity seen on color Doppler (A) and concentric blood vessels three-dimensional color Doppler image (B)

Tumor vascularity was traditionally thought of as a disease process intrinsic to the uterus, however, accumulating evidence suggests that fibroid growth may be linked with the systemic vasculature system (Kirschen, 2021). Moreover, fibroid vascularization correlates with absolute tumor volume change and also with fibroid growth rate per year (Seddon, 2011).

The standard clinical procedure for evaluation of fibroid vascularization is magnetic resonance imaging (MRI) with contrast. However, even very small vessels and blood flow in fibroids and their pseudocapsule can be also visualized with the use of color Doppler or power Doppler ultrasound. Volume and vascular-flow indices called VI, FI, VFI in uterine masses can also be calculated by 3D sonography using the manual contour tumor delineation (Perri, 2009; Testa, 2015). Nieuwenhuis et al. have found that in women with uterine fibroids without therapy, index of baseline vascularization (VI) measured with 3D power Doppler is correlated with absolute fibroid volume change at 12 months and with fibroid growth rate per year (Russo, 2022). The results of 3D sonographic vascularity assessment are highly dependent on image settings and experience of the operator and therefore may not be consistently reproducible. However, this imaging modality has been available for more than 20 years now and 3D ultrasound assessment of fibroid size and vascularity is much cheaper than MRI. Two examples of uterine fibroid vascularity on 3D sonographic imaging are presented below (Fig. 4A and B).

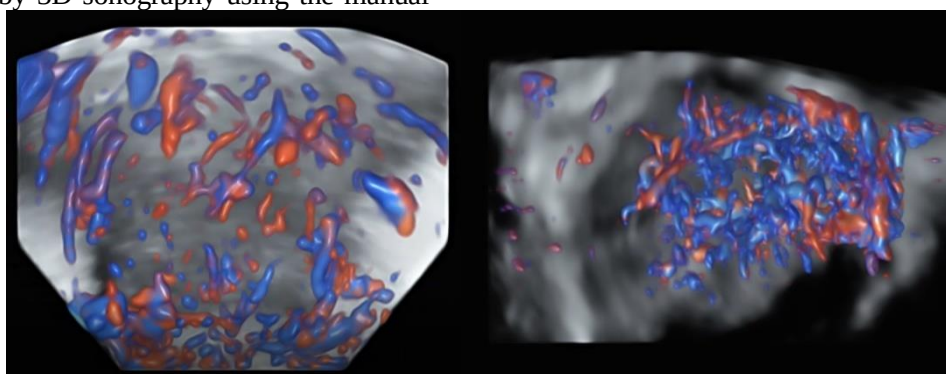

Figure 4. Transvaginal 3D imaging of a concentric vascularity on the periphery of uterine leiomyoma (A) and 3D image of abundant central vascularization within the oval-shaped uterine wall mass (B)

Although uterine fibroids are clonally derived from a single cell, despite being monoclonal, the cellular phenotypes that make up these lesions are heterogeneous consisting of predominantly smooth muscle cells (SMC) and fibroblasts (Ropacka-Lesiak, 2016). Depending of cell composition and the degree of internal degeneration fibroids may present complex echogenicity at ultrasound imaging. They may contain areas of solid parts adjacent to areas with fluid attenuation. When an acute necrosis occurs in a fast growing leiomyoma, at ultrasound examination more heterogeneous internal structures or internal sonolucent areas can be usually seen. When reviewing the ultrasonographic images in our database, we found that the features of these atypical uterine lesions could be classified into two main types: solid-

cystic and solid. Some rare benign smooth muscle cell derived masses like e.g. uterine fibromyolipoma display characteristic imaging findings that are due to the presence of internal fat. At pelvic sonography hyperechogencic and/or inhomogeneous echostructure is seen and resembles fat-containing dermoid cysts (Fig 5A). Another rare type, cellular leiomyoma is composed of compact smooth muscle cells with little or no collagen. Cellular leiomyomas are benign entity which may show imaging features of both degenerated leiomyoma and myometrial sarcoma. Typically at pelvic ultrasound, cellular leiomyoma is well defined without extra-myometrial invasion (Fig. 5B).

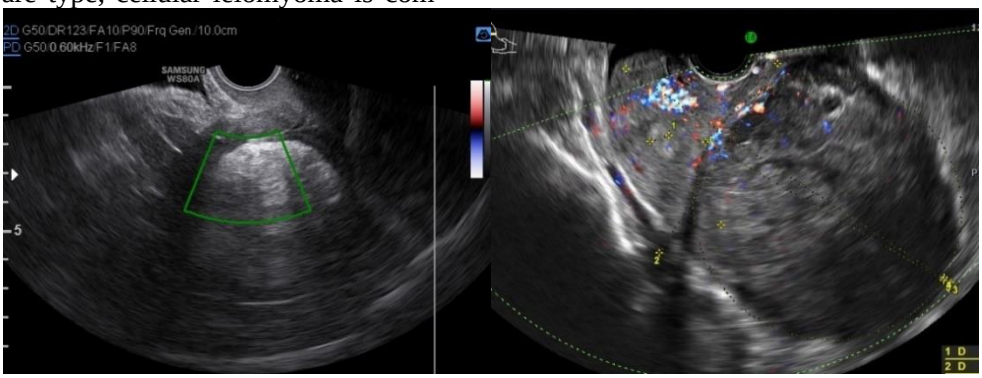

Figure 5. Transvaginal ultrasound images showing a hyperechogenic uterine lipoleiomyoma (A) and solid cellular leiomyoma (B). Transvaginal ultrasound shows in both cases uterine cervix (upper left corner) in a solid-cystic mass and solid lesion (B)

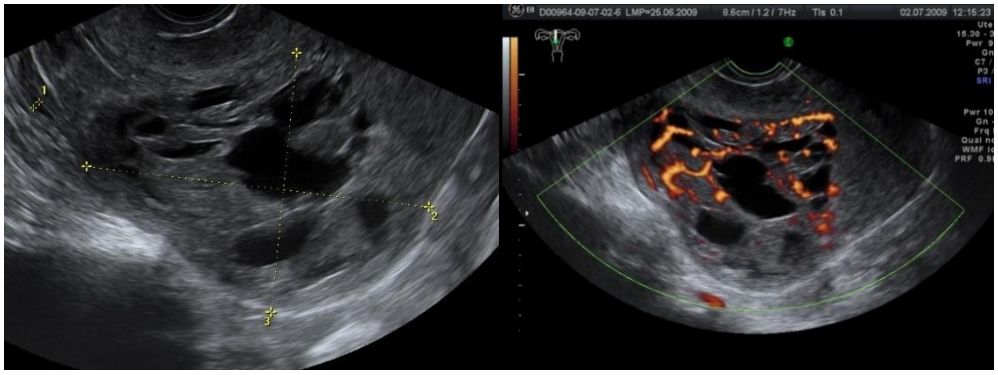

Figure 6. A case of degenerated cystic-solid leiomyoma (A) and cystic-solid, centrally vascularized angioleiomyoma (B)

In a vast majority of cases, transvaginal ultrasound combined with transabdominal scanning may clearly depict the uterine origin of fibroids. Nevertheless, some doubts may arise in cases of subserosal lesions that are pedunculated. These lesions may mimic other pelvic non-uterine masses. In particular, when uterine wall and cervix cannot be identified at pelvic sonography such atypical uterine lesions may be mistaken for multilocular adnexal cystic-solid tumors (Fig.7).

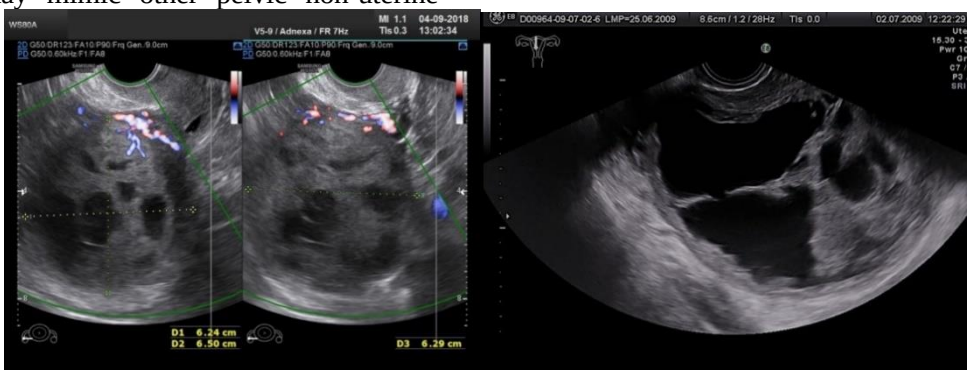

Figure 7. Two perpendicular images of atypical uterine fibroid with mixed internal echogenicity and multiple anechoic/fluid spaces (A) and a transvaginal gray-scale image of predominantly cystic multilocular mass with uneven internal margin's solid parts (B). No uterine clear structures were seen on pelvic sonography and both masses were mistakenly classified as probably malignant adnexal lesions

When sonographic assessment is difficult, such as in masses presented on Fig. 7, MRI is an extremely accurate tool for determining the anatomical origin of a pelvic mass. Particularly useful for this purpose are high-resolution T2-weighted images acquired orthogonal to the longest axis of the endometrium. In fact, the demonstration of conti-nuity of the pelvic mass with the adjacent myometrium enables the confirmation of its uterine origin, whereas the presence of a cleavage plane between the lesion and the adjacent myometrium helps exclude its uterine origin with certainty

ULTRASOUND FEATURES OF UTERINE SARCOMAS

Uterine sarcoma may occur spontaneously or, in rare cases, may be a result of malignant trans-formation of a pre-existing uterine leiomyoma. The specific preoperative diagnosis of uterine sarcomas is difficult and presents a real challen-ge for clinicians. Traditionally, it has been thought that a symptom indicating a high risk of sarcoma development is rapid growth of the "myoma". However, evidence from clinical studies suggests that the probability of uterine sarcoma in this clinical context is very low and does not exceed 0,1-0.23% [26]. The intro-duction of morcellation as a surgical technique in the laparoscopic removal of unexpected uterine sarcomas has made the clinical decisions even more difficult. Generally, the prognosis appears to be worse in women with latent uterine sarcomas that has been removed via laparoscopic morcellation (Perri, 2009).

Two-dimensional (2D) gray-scale sonography is currently the primary imaging modality used to evaluate presumably malignant uterine tumors. Color Doppler ultrasound may provide addi-tional information regarding the vascular pattern of the lesion. Testa et al. (Testa, 2015) have concluded that the detection of a large uterine myometrial tumor with inhomogeneous compact echogenicity, with irregular anechoic areas due to necrosis and absence of "radial stripy echogenicity" and with an irregular vasculari-zation could be suggestive of malignant myo-metrial lesions. Typical sonographic images of uterine sarcomas are presented in Fig. 8A and B.

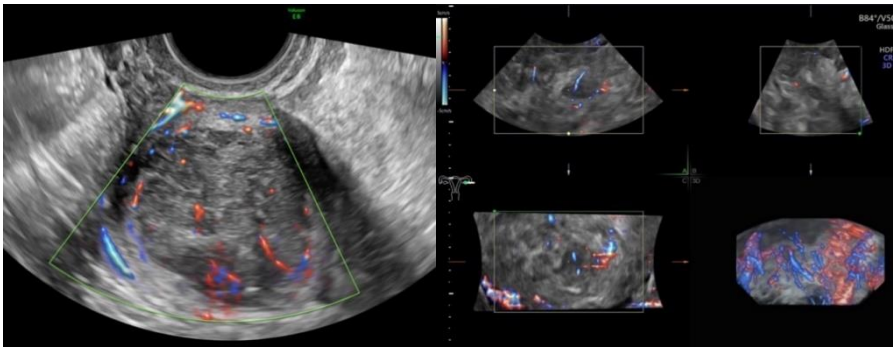

Figure 8. Typical ultrasound images of uterine leiomyosarcoma seen on 2D (A) and 3D (B) sonoangiography. Chaotic and central vessel arrangement within the mass can be better seen at three-dimensional blood flow imaging

Fig. 8 shows that at least in some cases several typical differences between LM's and LMSs like mixed echogenicity pattern and abnormal abundant tumor vascularity can be demonstrated on both 2D and three dimensional (3D) ultra-sound imaging. The additional use of 3D power Doppler blood flow and tumor vascularity assessment may provide additional information. The most recent analysis presented by Russo et al. (Russo, 2022) showed that ultrasound features of leiomyomas, such as circumferential and central lesion vascularity, cystic areas, and dimensions were all important parameters, especially when combined with the patient's age. These features were useful in the differen-tiation of typical uterine fibroids from malignant lesions in a pre-operative setting. However, our experience indicates that due to apparent overlap in imaging presentation between at least some atypical sarcomas and degenerated leiomyomas the ultrasound imaging may be misleading. Two examples of such difficult to differentiate uterine malignant tumors are presented on Fig. 9 and Fig. 10.

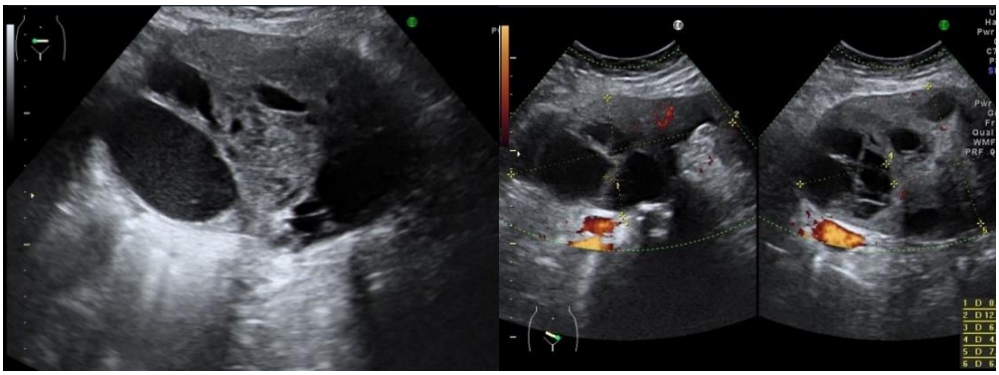

Figure 9. Atypical uterine cystic-solid leiomyosarcoma mimicking fibroid with mixed echostructure on gray-scale imaging (A) and at color Doppler blood flow mapping (B)

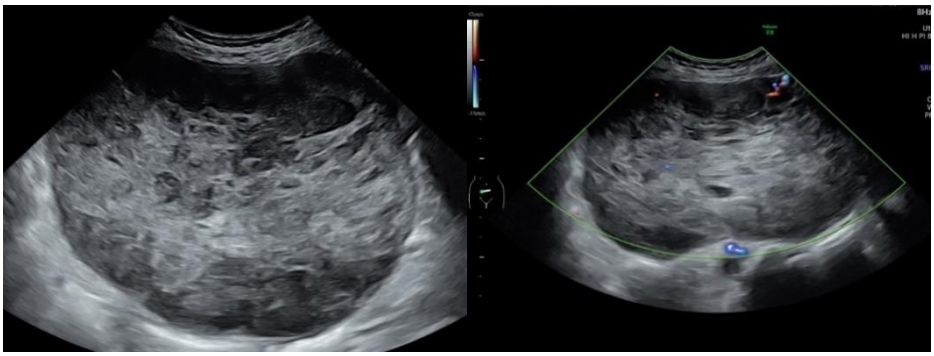

Figure 10. Atypical solid uterine leiomyosarcoma mimicking fibroid with mixed echostructure at gray-scale imaging (A) and at color Doppler where only scant peripheral vascularity could be seen (B)

SONOGRAPHIC IMAGING OF UTERINE SOFT TISSUE TUMORS OF UNKNOWN MALIGNANT POTENTIAL (STUMPS)

Atypical fibroids with unknown proliferation potential, called STUMPs comprise a group of relatively rare uterine lesion that do not have the characteristic clinical course. At imaging studies these tumors typically do not show malignancy features. However, because of their rarity and substantial variability of sonographic images, these masses should be differentiated with both leiomyomas and uterine sarcomas (Cotrino, 2022; Ropacka-Lesiak, 2016). As with the suspicion of sarcomas the final diagnosis should be only made after histopathological analysis. Fig. 11. presents a case of the histologically confirmed STUMP.

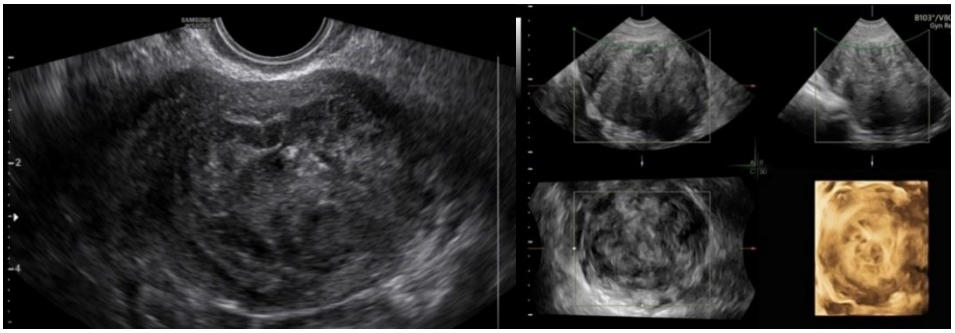

Figure 11. Transvaginal ultrasound image showing a tumor diagnosed finally as STUMP on gray–scale (A) and 3D imaging (B)

Mixed echostructure with internal shadowing, round, oval shape and scant vascularity suggested benign tumor. However, those ultrasonographic features have a low specificity and ultrasonography cannot be recommended as a reliable imaging modality to detect and characterize uterine STUMPS and atypical sarcomas. An open question remains if this lesion could be accurately predicted with the use of other imaging modalities. Apparently, when triaging these difficult cases of uterine tumors additional MRI imaging should be considered (Fujii, 2021; Aminzadeh, 2021). This observation is confirmed by the study of Amizandeh at al.

(Aminzadeh, 2021) who recently demonstrated that the marginal irregularity and/or ill-definition of lesion borders were highly reproducible observations for two independent, blinded observers reviewing a series of cases of LM, STUMPs and LMS. Marginal irregularity as well as DWI hyper/ADC hypointensity consistent with restricted diffusion was associated with 81% sensitivity and 78% specificity for LMS/STUMP.

SUMMARY

Uterine fibroids at ultrasound imaging present typically as well-defined, solid oval shaped masses. The lesions with a whorled appearance may resemble the echogenicity of the myometrium, but sometimes may be hypoechoic. Even non-calcified fibroids often show a degree of posterior acoustic shadowing. Although most cases have predictable sonographic features, for each histological entity there are some cases that do not exhibit typical features. The examples may include absence of vessels in a tumor solid parts seen on high resolution color Doppler, a relatively large solid vascularized part with no malignancy or smooth tumor margins in a malignant sarcoma. The appearance of non-typical morphology may also be due to physical limitations like e.g. the absence of Doppler signals when the distance between the ultrasound probe and the uterus is large. The difficulties may also be associated with abnormal uterus position over the symphysis pubis after cesarean section, histological characteristics, for example, presence of endometrial cysts in myometrium or other true outliers. The diagnostic accuracy of ultrasonography in differentiating between benign and malignant uterine masses has been shown to be dependent on the expertise of the sonographer.

The difficulties with the differentiation of atypical tumors at the time of the female pelvic structures imaging could result in misdiagnosis that in turn may lead to unwanted follow-up and treatment anxiety. Therefore, consultation with experienced centers should be the first step in the management of uterine masses with non-typical sonographic appearance. Because of apparent overlap in imaging features between degenerated leiomyoma and sarcoma, it is now suggested to consider collection of small tumor tissue sample from suspicious leiomyoma detected on pelvic and/or abdominal imaging. Biopsy samples are obtained transabdominally using "true-cut" method or using transcervical ultrasound-guided biopsy Following such biopsies histopathological and immunohistological analysis can be performed to improve diagnostic accuracy. Although time-consuming and costs incurred by biopsy it should be kept in mind that at least some of misdiagnosed uterine tumors may be fatal, and malignancy recurrence following conservative surgery is likely to happen. These women should also be closely monitored for possible complications that may happen during follow-up.

Finally, we conclude that although several tumor features on ultrasonography, CT and/or MRI can raise suspicion of a uterine malignant tumor, none of these modalities could provide a definitive diagnosis. Sonographic imaging and differentiation of uterine tumors presumed to be leiomyomas should always include a possible presence of other entities that could be atypical degenerated fibroids, adenomyosis, solid adnexal masses, focal myometrial contractions, and/or uterine leiomyosarcomas. "True-cut" or transvaginal ultrasound guided biopsy samples for immunohistochemistry should be considered before surgery in women with difficult to characterize solid or solid-cystic uterine lesions. Apart from MRI, newly designed studies based upon 3D ultrasound technologies will certainly be important in the precise evaluation of the future growth of typical and atypical fibroids and their potential response to medical and surgical treatments.

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