Malignant- mixed Müllerian tumors of the uterus: sonographic spectrum

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KEYWORDS: carcinosarcoma; mixed tumor; Müllerian; uterine neoplasm

ABSTRACT

Objective To describe the sonographic findings of malignant mixed Müllerian tumors (MMMTs) of the uterus with particular emphasis on their features on saline contrast sonohysterography (SCSH) and color Doppler sonography, and to determine how they relate to pathological findings.

Methods The SCSH and color Doppler findings in 29 histologically proven cases of uterine MMMT were reviewed retrospectively and their relationship to gross and histological findings were investigated.

Results Of the 29 uterine tumors, 16 were located in the corpus, nine in the fundus and four in both the corpus and fundus. Mean tumor size was 5.4 cm. The most common appearance was a polypoid mass projecting into the endometrial cavity, found in 23 cases. Twenty-eight tumors had an irregular surface, which was papillary in 20 cases and lobulated in eight. Most appeared heterogeneously isoechoic (n = 16) or hypoechoic (n = 12), occasionally with a trabecular appearance, and they often had clefts or fissure-like cystic areas (n = 10), necrosis (n = 4) or hemorrhagic areas (n = 7). Myometrial invasion was present in 27 cases and dilatation of the endometrial cavity was seen in 11. Color Doppler sonography showed moderate to marked vascularity in 20 cases with a mean resistance index of 0.41, which appeared as feeding (n = 15) or randomly dispersed (n = 9) vessels.

Conclusions Uterine MMMTs have distinct sonographic features that are related to pathological findings. Knowledge of the sonographic appearance of MMMTs may facilitate diagnosis. Copyright © 2012 ISUOG.

INTRODUCTION

Uterine malignant mixed Müllerian tumor (MMMT), also known as carcinosarcoma, is rarely encountered and accounts for only 1–3% of all uterine malignant tumors. It is a biphasic tumor that has both epithelial and stromal components. These tumors usually occur in elderly postmenopausal women, and tamoxifen treatment and prior pelvic radiotherapy have recently been recognized to be risk factors for the development of MMMT1–6.

Preoperative diagnosis of MMMT is important because the disease is usually diagnosed at an advanced stage with myometrial invasion and metastasis; hence, MMMT is associated with a poor prognosis. However, it is difficult to make the differential diagnosis of this tumor because of its rarity and lack of specific imaging features that might distinguish it from other malignant uterine tumors, including the more common endometrial carcinoma. Accordingly, the majority of MMMTs are diagnosed according to histological findings following endometrial curettage7.

Few case reports have described the sonographic appearance of MMMT. These reports describe a large, heterogeneous or hyperechoic intracavitary mass with dilatation of the endometrial cavity, or a diffuse mass replacing the uterus. Masses often have anechoic cystic areas or necrosis and prominent vascularity with randomly dispersed vessels. However, these are nonspecific findings, and overlap with endometrial carcinoma and other uterine sarcoma types7–14.

To the best of our knowledge, no review on the broad spectrum of sonographic appearances possible in uterine MMMTs has been undertaken, nor has any study been performed to investigate the relationship between sonographic features of MMMTs and histopathological findings to aid in the differentiation between MMMTs and other uterine tumors.

In this study, we aimed to describe the sonographic findings for MMMTs of the uterus, with particular emphasis on their features on saline contrast sonohysterography (SCSH) and color Doppler sonography, and to review the literature describing these features of uterine MMMTs.
Furthermore, we aimed to determine the relationship between these findings and histopathological findings.

PATIENTS AND METHODS

During the last 8 years, 29 women were histologically confirmed to have MMMT of the uterus at our institution. The average patient age was 61.1 (range, 33–69) years. The majority of patients were postmenopausal, and of the four premenopausal patients, one presented with polycystic ovarian disease. Patients with a history of estrogen replacement therapy, tamoxifen treatment or pelvic radiotherapy prior to imaging were excluded. Vaginal bleeding was present in 24 patients, vaginal discharge in two, pelvic pain in two and abdominal distension with weight loss in one. Serum CA-125 level was elevated in seven of the 26 patients tested, and results ranged from 40.7 to 1886 U/mL.

All 29 patients were examined by transvaginal sonography (TVS) and SCSH, and 24 were examined by color Doppler sonography prior to SCSH, using an Acuson Sequoia 512 system (Siemens Medical Solutions, Mountain View, CA, USA) with a 4–8-MHz endovaginal probe. Doppler parameters were adjusted as appropriate for optimal detection of low-velocity flow: Doppler frequency was 4–5 MHz; color gain was set at 40–50% with medium persistence; spatial peak temporal average intensity was set at c. 40–80 mW/cm²; the wall filter was set at 50–100 Hz; the pulse repetition frequency was set between 5 and 17 kHz; the velocity range was set at 4–20 cm/sec; the angle of insonation was maintained at less than 60 degrees; and the sample volume was 1–3 mm.

The sonographic findings of these tumors according to TVS and SCSH were evaluated retrospectively for the following characteristics: tumor location in corpus, fundus, or both; size; growth pattern (pedunculated, polypoid or broad-based sessile); surface (smooth or irregular, either lobulated or papillary); margins with underlying myometrium (ill-defined or well-circumscribed); echogenicity compared with myometrium (hyperechoic, isoechoic or hypoechoic) and echotexture (homogeneous or heterogeneous); the presence of cysts, hemorrhagic foci or necrosis; dilatation of the uterine cavity with fluid collection; the presence of myometrial invasion; and the presence of invasions to the cervix, adnexa and cul-de-sac. The tumor size was measured at its greatest diameter. Besides the presence of intratumoral cysts, ill-defined hypoechoic areas were understood to be suggestive of necrosis or hemorrhage. Myometrial invasion was determined by the poorly-defined endometrial–myometrial interface and the depth of myometrial invasion was classified into two categories according to previously defined criteria: superficial invasion of less than half of the myometrium and deep invasion of half of the myometrium or more. Direct tumor extension to the cervical stroma, and a discrete mass in the ovary or tube and on the peritoneal surface in the cul-de-sac were diagnosed as tumor invasion.

Tumor vascularity (mild, moderate or marked), vascular pattern (single or multiple, feeding or randomly dispersed vessels) and resistance index (RI) were also determined by color Doppler sonography. The RI of arterial flow in the main feeding and intraläsional vessels was recorded as the mean of measurements obtained from a minimum of three Doppler waveforms.

Surgical staging and pathological assessments were performed within 2 weeks of sonographic studies for all patients; nine patients had stage Ia disease, six had stage Ib, three stage IIa, five stage IIIc and six stage IVb. The pathological diagnoses of epithelial carcinoma in the 29 patients included 23 endometrioid adenocarcinomas, four papillary serous carcinomas, one mixed carcinoma, and one neuroendocrine carcinoma. The malignant stromal component was of the homologous type in 18 cases as endometrial stromal sarcoma or leiomyosarcoma, and was of the heterologous type in 11 cases as rhabdomyosarcoma, chondrosarcoma, osteosarcoma or liposarcoma. Pathological records of gross and histologic findings were correlated with sonographic findings. This study was approved by our Institutional Review Board and written informed consent was obtained from all patients.

RESULTS

TVS and SCSH revealed that 16 of the total 29 uterine tumors were in the uterine corpus, nine were in the fundus and four were in both the corpus and fundus. Tumor sizes ranged from 2.6 to 17 (mean, 5.4) cm. The most common appearance was a polypoid mass projecting into the endometrial cavity, which was found in 23 cases.

Four cases had pedunculated tumors and the remaining two had broad-based sessile masses. Twenty-eight tumors had an irregular surface that was papillary in 20 cases (Fig. 1) and lobulated in eight; the remaining tumor had a smooth surface.

The tumor appeared isoechoic relative to myometrium in 16 cases, hypoechoic in 12 cases and hyperechoic in one. Occasionally the tumors had a trabecular appearance and all had a heterogeneous echotexture (Fig. 2). Intratumoral clefs or fissure-like cystic areas were observed in 10 cases (Fig. 3) and other ill-defined hypoechoic areas suggestive of necrosis or hemorrhage were seen in four and seven cases, respectively.

In the 24 cases examined, color Doppler sonography depicted moderate to marked vascularity in 20 cases, and this appeared as single or multiple irregular feeding vessels entering though the pedicle in 15 cases (Fig. 4) or as randomly dispersed vessels in nine cases; RI values of these vessels ranged from 0.28 to 0.57 (mean, 0.41).

In 27 of the 29 cases, demarcation from underlying myometrium was poor, whereas in the remaining two cases tumors had a well-circumscribed margin. Myometrial invasion was observed in 27 cases; 16 cases showed superficial invasion and 11 deep invasion. On pathological examination, myometrial invasion was present in 28 cases, of which 12 cases were superficial and 16 were deep; the depth of myometrial invasion
MMMTs of the uterus

Figure 1 Malignant mixed Mullerian tumor in a 53-year-old woman. (a) Sagittal saline contrast sonohysterography image of the uterus showing a polypoid endometrial mass (3 × 2.6 cm) with a papillary surface that projects into the endometrial cavity in the fundus. (b) Hysterectomy specimen showing a fungating tumor arising from the fundus that fills the uterine cavity, with lobulations and characteristic leaf-like projections on the external surface.

was underestimated on ultrasound in four cases and overestimated in three.

As for other sonographic findings, dilatation of the endometrial cavity and fluid was observed in 11 cases. Cervical invasion was present in five cases and adnexal invasion with a mass in the ovary and/or tube was present in 10 cases; these findings correlated well with the gross and histological findings. Three cases had fluid in the cul-de-sac and five had masses on the pelvic peritoneal surface; in eight cases the cytological result of peritoneal washing was positive and pelvic peritoneal metastases were revealed.

DISCUSSION

Uterine MMMTs arise from the endometrium, most commonly in the uterine fundus, but rare tumors may arise in the uterine cervix. This type of tumor is typically a large fungating mass that usually fills the uterine cavity and occasionally prolapses through the cervical os. Its cut surface is usually fleshy with blunt polypoid projections on the external surfaces, which often show areas of hemorrhage, necrosis and cystic changes. Myometrial invasion is frequently observed. The tumor extends to the endocervix in 25% of cases\(^1\)\(^-\)\(^3\). Definite diagnosis of the disease is usually made by performing curettage, but it is often difficult to make a specific preoperative diagnosis because, in most cases, an endometrial biopsy can indicate either carcinoma or sarcoma. Preoperative radiological diagnosis is somewhat limited by the rarity of MMMTs, and the lack of specific imaging findings prevent distinguishing them from other malignant tumors of the uterine corpus\(^7\).

The sonographic findings for these tumors have rarely been reported in the literature. In a few case reports, their transvaginal sonographic appearance has been variably...
Figure 3 Malignant mixed Mullerian tumor in a 69-year-old woman. (a) Transverse saline contrast sonohysterography image showing a polypoid mass (4.2 × 3.5 cm) with a well-defined cleft-containing or fissure-like cystic area in the posterior corpus. (b) Cut section of the resected tumor showing central, broad or branching clefts measuring 0.3–1.0 cm. (c) Photomicrograph (original magnification, × 10) showing polypoid or leaf-like protrusions of sarcomatous stroma displaying cartilaginous differentiation into cystically dilated malignant glands.

Figure 4 Malignant mixed Mullerian tumor in a 57-year-old woman. (a) Sagittal color Doppler image of the uterus showing a single feeding vessel at the base of the tumor. (b) Cut surface of the resected tumor showing a large feeding vessel, which typically entered through the pedicle, and branching small vessels within the mass.

Two patterns of sonographic appearance have been previously identified in cases of uterine MMMT, with the tumor presenting as either an intracavitary polypoid mass or a diffuse mass replacing the uterus. In addition, a homogeneous echogenic minimal diffuse thickening of the endometrium has been described as a less common presentation, and a pedunculated lesion protruding into the endocervical canal has also been described. A recent case of MMMT arising from an endometrial polyp presented as a heterogeneous, thickened well-defined endometrium with some cystic areas and the myometrial–endometrial interface was well defined. Another case of a tamoxifen-induced MMMT that appeared as a small cavitary polyp has also been reported. The majority of intracavitary masses are heterogeneous or hyperechoic, often with anechoic cystic areas or necrosis, and have in common myometrial invasion and frequent extension into the endocervix.

A few case studies have reported the vascular features of MMMTs as assessed by Doppler sonography. These reported the vascular features of MMMTs as assessed by Doppler sonography. These described as a large intracavitary mass with expansion of the endometrial cavity and myometrial invasion or as a bulky mass replacing the entire uterus with a contiguous extrauterine mass in the adnexa and cul-de-sac.
tumors typically show prominent vascularity, which appears as irregular thin and randomly dispersed vessels in either peripheral or central areas, or both, and low impedance\(^{12}\), confirming previous findings in uterine sarcoma reported by Kurjak et al.\(^{13}\). However, another study reported that vascularization is mainly peripheral and tumor hypervascularity is not shown\(^7\). A more recent report described 3D power Doppler findings that showed a highly vascularized lesion with a main feeding vessel and abnormal branching patterns\(^{14}\).

In the present study, most tumors involved the uterine corpus and less commonly the fundus. MMMTs were usually polypoid masses, but occasionally presented with pedunculation, and some were sessile. These findings are rather similar to those of previous reports that described the two sonoagraphic patterns. However, almost all tumor lesions in our cases were polypoid, which has been reported to be more common\(^8\), and no diffuse mass lesion replaced the uterus. In addition, we found that growth of a pedunculated lesion into the endocervical canal was rare. With the exception of only one tumor with a smooth surface, tumor surfaces were irregular in all cases, and showed typical papillary contours that represented blunt polypoid, exophytic projections on the external surfaces on gross examination. The papillary nature of tumor surfaces, demonstrated in our cases of uterine MMMT, might be one of the characteristic imaging findings for these tumors.

Tumor echogenicities were mostly heterogeneously isoechoic or hypoechoic, often with a trabecular appearance, interspersed with hyperechoic areas. Histopathological examinations showed that these areas, hypoechoic to isoechoic by ultrasound, appeared to correspond to regions of predominantly sarcomatous tissue, which was arranged in a trabecular pattern with interfacing spindle-cell fascicles, whereas the areas of high echogenicity chiefly corresponded to carcinomatous tissue containing glandular structures. Previous case reports have described the hyperechogenicity and heterogeneous echotexture of this tumor, as was observed in the present study\(^8\)–\(^{10}\), but we rarely observed a predominantly hyperechoic mass.

The presence of clefts or fisurlike cystic areas revealed by ultrasound is the most distinctive difference between our findings and those of previous reports. Pathological examinations revealed these cystic areas to be endophytic protrusions of malignant stroma into cystically dilated glands lined by malignant epithelium; the appearances of intraglandular protrusions ranged from round-like minor indentations to polypoid leaf-like protrusions. Ill-defined anechoic to hypoechoic intratumoral areas were also common and corresponded to areas of focal hemorrhage or necrosis as determined by gross and pathological examinations.

In the present study, MMMTs usually had feeding vessels, which typically entered through the pedicle, and contained small branching vessels, which were also evident on gross examination; these findings are compatible with those of prior reports\(^{12}–^{14}\). Color Doppler sonography depicted marked vascularity in the hypoechoic solid areas of tumors. We suggest that this prominent vascularity relates to hypoechoic areas revealed by ultrasound and presume that it could correspond to the multiple thick-walled, large blood vessels in sarcomatous regions found during histologic examinations (Fig. 5). However, these findings contradict an earlier observation of a higher degree of neovascularization in the epithelial than in the mesenchymal component\(^{12}\). MMMTs usually exhibit a poorly defined margin with underlying myometrium and myometrial invasion. Invasion to the adnexa and pelvic peritoneum metastasis in the cul-de-sac also were found frequently. These findings are similar to those of previous reports\(^8\)–\(^9\). However, dilatation of the endometrial cavity and cervical invasion were relatively uncommon in our study.

In summary, we found that sonography revealed distinct features in uterine MMMTs that corresponded well with gross and microscopic pathological findings.
REFERENCES


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Queries to Author:

AQ1 Please confirm suggested short title, or amend. (JC)

AQ2 Please check that all affiliations are correct and complete.

AQ3 ‘sonohysterography (SH)’ expanded to ‘saline contrast sonohysterography (SCSH)’ throughout in line with Journal style, is that correct? (OS)

AQ4 ‘The tumor surface was lobulated and more frequently papillary in 28 of the 29 cases’ this sentence did not seem entirely clear to me, so I have changed it to ‘Twenty-eight tumors had an irregular surface, which was papillary in 20 cases and lobulated in eight’ as in the main Results, ok? (OS)

AQ5 ‘resistive index’ changed to ‘resistance index’, ok? (OS)

AQ6 ‘During the last 8 years,’ could you provide the date range considered? (OS)

AQ7 ‘the velocity range lowered to 4 to 20 cm/sec’, would it be correct to change this to ‘the velocity range was set at 4 to 20 cm/sec’? (OS)

AQ8 ‘ill-defined hypoechoic areas were defined as suggestive of’ was changed to ‘ill-defined hypoechoic areas were understood to be suggestive of’; please confirm. (JC)

AQ9 ‘In 27 of the 29 cases, demarcation from underlying myometrium was poor, whereas in the remaining 2 cases tumors had a well-circumscribed margin. Myometrial invasion was observed in 27 cases; 16 cases showed superficial invasion and 11 deep invasion.’, is this section describing findings on both TVS and SCSH, could this be specified here? (OS)

AQ10 ‘positive peritoneal washing cytologic result and pelvic peritoneal metastasis were found in 8 cases on pathological finding’ was changed to ‘in eight cases the cytological result of peritoneal washing was positive and pelvic peritoneal metastases were revealed’ (‘on pathological finding’ was deleted because it seemed perhaps redundant; please confirm or amend. (JC)

AQ11 ‘Two sonographic patterns were identified previously in cases of uterine MMMT as an intracavitary polypoid mass and a diffuse mass replacing the uterus’ reworded to ‘Two patterns of sonographic appearance have been previously identified in cases of uterine MMMT, with the tumor presenting as either an intracavitary polypoid mass or a diffuse mass replacing the uterus’, is that correct? (OS)

AQ12 ‘In addition, a homogeneous echogenic minimal diffuse thickening of the endometrium was the uncommon appearance6,8 and a pedunculated lesion protruding into the endocervical canal has been described12’ reworded to ‘In addition, a homogeneous echogenic minimal diffuse thickening of the endometrium has been described as a less common presentation6,8, and a pedunculated lesion protruding into the endocervical canal has also been described12’, is that correct? (OS)

AQ13 ‘this hypoechoic to isoechoic areas by ultrasound’ was changed to ‘these areas, hypoechoic to isoechoic by ultrasound’, please confirm or amend. (JC)

AQ14 Please confirm the slight change in your final sentence, or amend. (JC)
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