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Ultrasonographic appearance of metastatic non-gynecological pelvic tumors

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KEYWORDS: metastatic ovarian tumors; metastatic pelvic tumors; ultrasound diagnostics

ABSTRACT

Objective *To describe the ultrasound (sonomorphologic and vascular) characteristics of metastatic non-gynecological pelvic tumors, and to identify ultrasound characteristics typical of the most common non-gynecological pelvic tumors.*

Methods *In 92 patients with a pelvic mass who had undergone ultrasound examination with subsequent surgery or tru-cut biopsy revealing a metastatic non-gynecological tumor origin, we analyzed retrospectively the sonomorphologic and vascular parameters. All parameters were evaluated for the whole group of non-gynecological tumors as well as separately for each specific tumor type. The findings were compared with those from 100 women with epithelial ovarian cancer.*

Results *We found that CA 125, size of tumor, echogenicity, homogeneity of solid portion, mobility, and presence of ovarian crescent sign, parenchymal metastases and suspicious necrosis were individual statistically significant discriminators ($P < 0.01$) between the metastatic non-gynecological tumor group and the epithelial ovarian cancer group.*

Conclusions *Metastatic non-gynecological tumors in the pelvis have a significantly different sonomorphologic pattern compared with primary epithelial ovarian cancer. This pattern is dependent on the primary origin of the tumor. Doppler parameters, however, cannot differentiate between primary ovarian cancer and metastatic non-gynecological tumors. Copyright © 2012 ISUOG. Published by John Wiley & Sons, Ltd.*

INTRODUCTION

Patients with a pelvic mass are commonly referred to a gynecologic oncology center for expert ultrasound examination due to suspected gynecologic cancer. Sonography is the first method of choice for identifying the location of a tumor and its origin, and to distinguish between benign and malignant tumors; the ultrasound probe can get close to the tumor and Doppler can be used to assess parameters of vascularization[10]. However, the pelvis, and the ovaries in particular, is often the site of metastases from extragenital (i.e. non-gynecological) malignant tumors. Metastatic extragenital tumors constitute 5–20% of all ovarian tumors[1–4]; according to the literature, they are most commonly derived from gastric or breast cancer[4,5]. The recognition preoperatively of a potential extragenital origin of a tumor can significantly change the management of the patient and allow for early initiation of appropriate treatment of the primary disease[8,9]. Yet, only a few studies have evaluated the accuracy of ultrasound examination in determining the extragenital origin of tumors[5–7]. According to their conclusions, a large proportion of metastatic ovarian tumors are misinterpreted as being primary ovarian epithelial cancer.

The aim of this retrospective study was to analyze sonomorphological and vascular parameters of non-gynecological metastatic pelvic tumors and to assess the presentation of all tumor types and their typical ultrasound features in comparison to those of ovarian epithelial cancer.

METHODS

Patients

The study population included 92 patients referred to the Gynecologic Oncology Center from 2005 to 2009 who underwent expert ultrasound examination and in whom a pelvic mass of non-gynecologic origin was subsequently confirmed and identified by histology (open surgery,

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laparoscopy or tru-cut biopsy). Patients in whom a non-gynecologic origin of the pelvic tumor had been assumed on the basis of computed tomography or magnetic resonance imaging findings, were not enrolled into the study. Primary peritoneal serous tumors are classified as genital tumors, so these patients were not included in the study. Ovarian tumors with metastases to the uterus, tumors of the uterus with metastases to the ovaries and tumors growing from other pelvic structures and penetrating the uterus and ovaries were also not included.

For comparison, we enrolled a group of 100 patients suffering from epithelial ovarian cancer and examined with ultrasound (four Stage IV, 72 Stage III, 17 Stage II and seven Stage I) using the same scan protocol as for the study group. Eighty of them had serous histotype cancer, 10 had clear cell cancer, six had endometrioid cancer and four had mucinous cancer. All 100 underwent surgery.

Ultrasound examination

Each patient underwent both transabdominal and transvaginal or transrectal ultrasound examination, performed by one of two oncogynecologists experienced in the field of ultrasound diagnostics in gynecologic oncology, using a GE Logiq 9 (GE Healthcare Ultrasound, Milwaukee, WI, USA) machine equipped with a M7C matrix 3–8-MHz transducer and with both B-mode and Doppler mode. The description and examination reports were based on the standard protocol for pelvic mass evaluation applied by our center and using the terminology described previously[11] (Table 1). The still images and videoclips taken during the course of the examination were stored in electronic form.

Evaluation of acquired data

Our assessment was carried out retrospectively by reviewing the stored examination reports. In cases of uncertainty or lack of clarity in the report, stored still images or videoclips were used to clarify, without knowledge of the histological diagnosis.

There was no tumor duplicity. Tumors metastasizing to the ovaries were designated as ovarian (there were no tumors affecting the corpus uteri or cervix uteri). If the tumor was confined to the ovarian surface only, with unaffected ovarian stroma, it was classified as non-ovarian with carcinomatosis. Tumors fixed to the pelvic wall, supplied by external, internal or common iliac artery, or tumors clearly located below the parietal peritoneum, were classified as retroperitoneal. Heterogeneous, avascular areas of mixed echogenicity with blurred borders radiating to the adjacent vascularized tissue were classified as probable necrosis (Figure 1).

The elasticity of tumors was assessed using pressure exerted by the vaginal probe with simultaneous abdominal wall palpation (in order to avoid moving the tumor) and classified as compressible or rigid.

The mobility of tumors was assessed by their movement with respect to the adjacent structures when the examiner's hand was pressing on the abdominal wall with simultaneous scanning by transvaginal or transabdominal ultrasound probe. A tumor was considered mobile when

Table 1 Scan protocol: summary of characteristics examined during routine scanning of pelvic masses

Characteristic
Location
Ovarian
Non-ovarian (intraperitoneal; retroperitoneal)
Laterality
Unilateral
Bilateral
Solitary central
Size (measured in three dimensions)
Size of largest solid component (if applicable)(measured in three dimensions)
Distribution
Pelvic
Pelvic and extrapelvic
Structure
Solid
Unilocular-solid
Multilocular-solid
Unilocular
Multilocular
Papillary projections (yes/no)
Echogenicity
Anechoic
Low level
Ground glass
Hemorrhagic
Mixed
Homogeneity of solid portion (if applicable) (yes/no)
Vascular features of solid portion (if applicable)
Subjective assessment of flow (1–4)[11]
Peak systolic velocity
Pulsatility index
Resistance index
Surface
Smooth
Irregular
Elasticity
Compressible
Rigid
Mobility
Mobile
Semi-fixed
Fixed
Ovarian crescent sign (yes/no)
Locularity (if applicable)
Number of locules (1–5; 6–10; > 10)
Size of chambers
Septa (if applicable)
Width
Regularity of width
Subjective assessment of flow (level 1–4)[11]
Suspicious necrosis (yes/no)
Involvement of uterus (yes/no)
Presence of carcinomatosis (yes/no)
Ascites (yes/no)
Parenchymal metastases (yes/no)

Parameters were evaluated/measured in each patient (if applicable) and expressed in words according to the institute's documentation and also stored as images or videoclips.

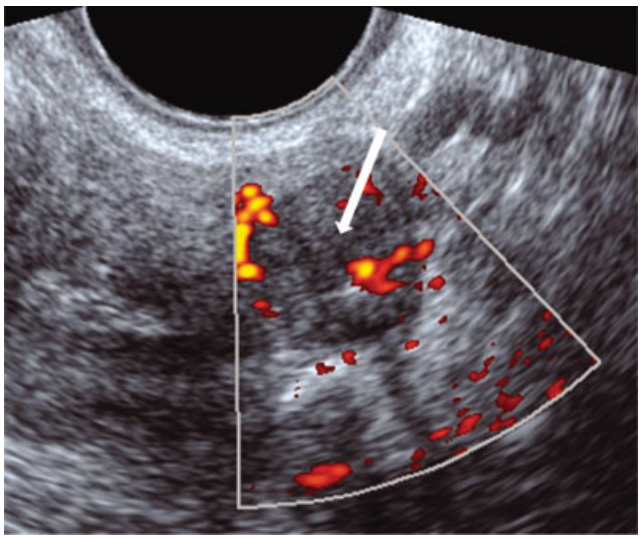

Figure 1 Necrosis: heterogeneous irregular avascular area (arrow) surrounded by vascularized tissue.

it moved freely all around its perimeter in relation to the adjacent structures, semi-fixed if it was firmly attached by at least part of its perimeter or the adjacent structures did not show any sliding, and fixed if it was completely immobile.

For each of the parameters assessed, its frequency in the particular group of tumors was expressed as a percentage. For certain selected parameters, their frequency among all assessed tumors was calculated.

Statistical analysis

Hotelling's distribution model (a modification of Student's model) was used for parametric testing, comparing all variables for metastatic vs primary tumors. Variables for individual subgroups of metastatic tumors were compared with those in the primary ovarian cancer group using ANOVA, Fisher's exact test or multivariate regression analysis based on OPLS (orthogonal projection to latent structure) model, depending on data categories and distribution.

RESULTS

Of the 92 patients with metastatic malignant tumor of non-gynecological origin included in this study, 39 (42.4%) were diagnosed by surgery and 53 (57.6%) by biopsy. All had undergone ultrasound examination at our department and the findings led the investigator to suspect the metastatic tumor of non-gynecologic origin in 75 (81.5%) of them. Previous non-gynecologic tumor was reported by 23 (25%) of the patients. The tumor marker CA 125 level was above the cut-off value (35 kIU/L) in 47 patients (51.1%). The average value in these patients was 83.2 kIU/L (range, 41.2–438.4 kIU/L).

Among the metastatic non-gynecologic tumors, by far the most common type on histology was colorectal cancer, which was identified in around one third of patients. The types and frequencies of individual tumors is given in Table 2.

Table 2 Type and frequency of non-gynecological tumors in the study group

Tumor	*Patients (n (%))*
Colorectal cancer	32 (34.8)
Upper gastrointestinal tract (pancreas, gallbladder) tumor	13 (14.1)
Lymphoma	11 (11.9)
Krukenberg tumor (metastatic gastric cancer)	9 (9.8)
Breast cancer	6 (6.5)
Gastrointestinal stromal tumor	4 (4.3)
Urinary bladder cancer	3 (3.3)
Neuroendocrine tumor	2 (2.2)
Carcinoid tumor	2 (2.2)
Malignant mesothelioma	1 (1.1)
Malignant Schwannoma	1 (1.1)
Primitive neuroectodermal tumor	1 (1.1)
Liposarcoma	1 (1.1)
Leiomyosarcoma	1 (1.1)
Ewing's sarcoma	1 (1.1)
Thyroid cancer	1 (1.1)
Perimyocytoma*	1 (1.1)
Atypical retroperitoneal leiomyoma*	1 (1.1)
Pseudomyxoma peritonei (malignant)	1 (1.1)

Diagnosis was made from histopathologic evaluation (surgery or tru-cut biopsy). *Tumors with unclear biological behavior.

General characteristics of non-gynecological tumors

We found that intraperitoneal tumors prevailed over retroperitoneal tumors (84/92 (91.3%) vs 8/92 (8.7%)). Among the intraperitoneal tumors, 39/84 (46.3%) had an ovarian location; the remaining 45 (53.7%) were on the parietal or visceral peritoneum or in the adnexal region outside the ovaries. Intraperitoneal tumors were most often unilateral (73/84 (87.0%)). There was a wide range of sizes (largest diameter; range, 20–300 (mean, 120) mm).

Extrapelvic pathology, i.e. detection using transabdominal ultrasound of presence of a tumor above the level of the pelvis (apart from parenchymal metastases), was observed in 23/92 (25.0%) tumors.

Structurally, tumors were mostly solid (49/92 (53.3%)) or multilocular-solid (38/92 (41.3%)); a small proportion of tumors was unilocular-solid (5/92 (5.4%)). There were no tumors without a solid component. When there were septa (in multilocular-solid tumors), these were always vascularized and irregular in width; in the majority (35/38 (92.1%)), the septa were > 5 mm in width. Papillary projections were found rarely, being recorded only in cases of colorectal cancer metastases (10/32 (31.3%)).

A combination of gray-scale and Doppler changes which led us to suspect necrosis was observed in more than half (47/92 (51.1%)) the tumors. A high rate of suspicious necrosis was detected in the solid portion in particular (in 36/43 (83.7%) locular tumors with a solid component). In the majority of cases the solid component of locular tumors was heterogeneous (i.e. mixed echogenicity)

(34/43; 79.2%). In 20 of the 47 patients with potential necrosis, tru-cut biopsy was performed, while the remaining 27 patients underwent surgery. In patients who underwent surgery, the histological report explicitly described necrosis in 25 (92.6%) cases. We used histopathologic reports of initial clinical assessments and were thus able to verify this parameter in only 25/47 (53.2%) cases of necrosis suspected on the basis of ultrasound. In addition, necrosis was found on histopathological examination in two (16.7%) of the remaining 12 patients who underwent surgery, but in whom ultrasound findings suspicious for necrosis were not reported. However, on multivariate regression analysis, this variable was a significant discriminator between metastatic non-gynecological and epithelial ovarian tumors ($P < 0.01$) (Table 3).

On subjective assessment, tumor vascularization was given a mean score of 3. Both resistance index (RI) < 0.4 and pulsatility index (PI) < 0.6 (as the threshold values for recognition of low-resistance vessels) were reported in 65/92 (70.6%) tumors. Peak systolic velocity (PSV) ranged from 7.7 to 30.9 (mean, 15.1) cm/s.

When pressure was applied using the vaginal probe, only 24/92 (26.1%) tumors were compressible, whereas the majority of them (68/92 (73.9%)) were rigid. Twenty of 92 (22.5%) tumors were fixed, 38/92 (40.8%) were semi-fixed and 34/92 (36.6%) were mobile.

Carcinomatosis was detected in one quarter of tumors only, all in combination with ascites (21/92; 22.8%). Parenchymal metastases were observed in 31/92 (33.7%) tumors, with all cases being liver metastases. Ascites was present in 85.9% (79/92) of patients.

In the statistical evaluation using Hotelling's distribution model, regarding all the variables together, the group of metastatic non-gynecological tumors differed significantly from the group of epithelial ovarian cancers ($P < 0.0001$). Table 3 gives proportions and statistical significance for individual variables in specific non-gynecological and primary ovarian tumors.

We found that CA 125, size of tumor, echogenicity, homogeneity of solid portion, mobility, presence of ovarian crescent sign, presence of parenchymal metastases and suspicion of necrosis were individual statistically highly significant ($P < 0.01$) discriminators between the group of metastatic non-gynecological tumors and the epithelial ovarian cancer group (Table 3).

Metastatic colorectal cancer

Typical features of metastatic colorectal cancers based on subjective assessment were a layered structure in the caudal part of the tumor, the presence of papillary projections and the presence of necrosis in the hypoechogenic solid portion. Tumors had predominantly hyperechogenic septa with a mostly hypoechogenic heterogeneous solid portion. Isoechogenic to hyperechogenic papillary projections growing from thin septa, which are specific for colorectal metastases, were observed in 5/32 (15.6%) tumors (Figure 2).

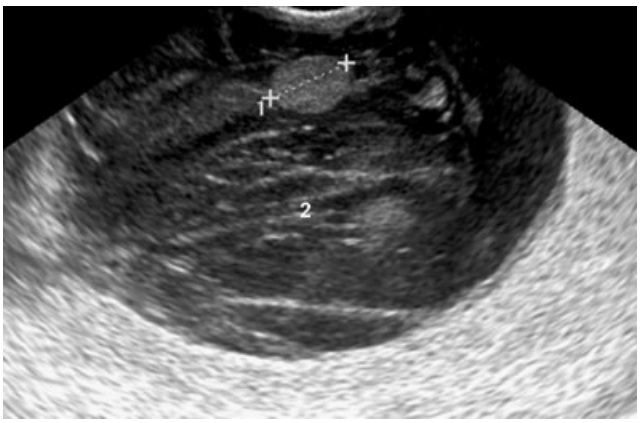

Figure 2 Metastasis of colorectal cancer: multilocular-solid tumor with typical layered structure (2) with papillary projections from septa (1).

Colorectal cancer metastases to pelvis differed highly significantly ($P < 0.01$) from the primary ovarian cancer group in structure, surface, size, presence of carcinomatosis, ascites, parenchymal metastases and presence of necrosis (Table 4). In the prediction model these variables distinguished between metastatic non-gynecological tumors and epithelial ovarian cancer with a sensitivity of 90.6% and specificity of 97.9%.

Upper gastrointestinal tract – metastatic gallbladder, bile duct and pancreatic cancer

Metastatic pelvic masses derived from primary cancer of gallbladder, bile ducts or pancreas typically exhibited multilocular-solid structure with numerous small locules of irregular size and, compared with metastases from colorectal cancer, had smaller solid components, without necrosis. The tumors were of mixed echogenicity: hyperechogenic septa with isoechogenic to hyperechogenic solid component, and individual components manifested a heterogeneous pattern (Figure 3). Tumors and septa were richly vascularized.

Upper gastrointestinal tract metastases to the pelvis differed highly significantly ($P < 0.01$) from the primary ovarian cancer group in distribution, echogenicity, homogeneity, surface, elasticity and mobility (Table 4). In the prediction model these variables distinguished between metastatic non-gynecological tumors and epithelial ovarian cancer with a sensitivity and specificity of 100.0%.

Lymphoma (non-Hodgkin lymphoma only)

Typically, non-Hodgkin lymphoma in the pelvis had a retroperitoneal location, solid structure and strongly heterogeneous map-like internal structure with alternating minor hyperechogenic and hypoechogenic areas (Figure 4). Tumors were richly vascularized.

Tumors differed highly significantly ($P < 0.01$) from the primary ovarian cancer group in laterality, structure, echogenicity, homogeneity, presence of ovarian crescent sign and necrosis (Table 4). In the prediction model

Table 3 Characteristics of five most common metastatic tumors in our study group, and differences between metastatic non-gynecological and epithelial ovarian cancer as evaluated by multivariate regression*

Demographic, clinical or ultrasound variable	*Metastatic non-gynecological tumor origin*					*Epithelial ovarian cancer*	*Multiple regression parameter (95% CI)*	P
	Colorectal cancer	*Upper gastrointestinal tract†*	*Lymphoma*	*Krukenberg tumor*	*Breast cancer*			
Patient age (years)	70 (37–96)	65 (42–86)	55 (31–85)	50 (38–86)	58 (46–66)	57 (41–85)	0.006 (−0.107 to 0.119)	NS
CA 125 (kIU/L)	95 (33–246)	67 (12–98)	28 (15–94)	63 (29–127)	93 (36–186)	272 (6–6891)	0.246 (0.166 to 0.326)	< 0.01
Location							0.105 (−0.005 to 0.215)	NS
Ovarian	16/32 (50.0)	12/13 (92.3)	2/11 (18.2)	9/9 (100)	2/6 (33.4)	86/100 (86.0)		
Non-ovarian intraperitoneal	16/32 (50.0)	1/13 (7.7)	0/11	0/9	4/6 (66.6)	14/100 (14.0)		
Retroperitoneal	0/32	0/13	9/11 (81.8)	0/9	0/6	0/100		
Laterality							0.043 (0 to 0.086)	NS
Unilateral	30/32 (93.8)	12/13 (92.3) (all ovarian)	10/11 (90.9) (incl. both ovarian)	8/9 (88.9) (ovarian)	2/6 (33.4) (ovarian)	47/100 (47.0)		
Bilateral	2/32 (6.2) (both ovarian)	1/13 (7.7)	0/11	1/9 (11.1) (ovarian)	4/6 (66.6)	53/100 (53.0)		
Solitary central	0/32	0/13	1/11 (9.1)	0/9	0/6	0/100		
Size (max. diameter, cm)	10.5 (4–30)	15 (5–20)	9 (3–18)	6 (3–30)	9¶	5 (2–16)	−0.151 (−0.202 to −0.1)	< 0.01
Largest diameter > 10 cm	16/32 (50.0)	11/13 (84.6)	6/11 (54.5)	0/9§	0/2			
Distribution							−0.029 (−0.089 to 0.031)	NS
Pelvic	29/32 (90.6)	6/13 (46.2)	10/11 (90.9)	8/9 (88.9)	1/6 (16.7)	36/100 (36.0)		
Pelvic and extrapelvic	3/32 (9.4)	7/13 (53.8)	1/11 (9.1)	1/9 (11.1)	5/6 (83.3)	64/100 (64.0)		
Structure							0.055 (−0.019 to 0.129)	NS
Solid	11/32 (34.3)	0/13	11/11 (100)	9/9 (100)	6/6 (100)	52/100 (52.0)		
Unilocular–solid	2/32 (6.3)	0/13	0/11	0/9	0/6	22/100 (22.0)		
Multilocular–solid	19/32 (59.4)	13/13 (100)	0/11	0/9	0/6	26/100 (26)		
Unilocular	0/32	0/13	0/11	0/9	0/6	0/100		
Multilocular	0/32	0/13	0/11	0/9	0/6	0/100		
Papillary projections	5/32 (15.6)	0/13	NA	NA	NA	20/100 (20.0)	0.081 (0.017 to 0.145)	< 0.05
Echogenicity							−0.291 (−0.315 to −0.267)	< 0.01
Anechoic	0/32	0/13	0/11	0/9	0/6	0/100		
Low level	6/32 (18.8)	0/13	0/11	0/9	0/6	90/100 (90.0)		
Ground glass	2/32 (6.2)	0/13	0/11	0/9	6/6 (100)	2/100 (2.0)		
Hemorrhagic	0/32	0/13	0/11	0/9	0/6	0/100		
Mixed	24/32 (75.0)	13/13 (100)	11/11 (100)	9/9 (100)	0/6	8/100 (8.0)		
Homogeneous solid portion	1/32 (3.1)	0/13	0/11	0/9	6/6 (100)	89/100 (89.0)	0.263 (0.222 to 0.304)	< 0.01
Vascular features of solid portion							0.000 (−0.033 to 0.033)	NS
Subjective assessment of flow (1–4)[11]	3 (2–3)	3 (3)	3 (3)	3 (2–3)	3 (2–3)	3 (1–3)		

Table 3 (*Continued*)

Demographic, clinical or ultrasound variable	*Metastatic non-gynecological tumor origin*					*Epithelial ovarian cancer*	*Multiple regression parameter (95% CI)*	P
	Colorectal cancer	*Upper gastrointestinal tract†*	*Lymphoma*	*Krukenberg tumor*	*Breast cancer*			
Subjective vascular intensity score of 3	31/32 (96.9)	13/13 (100)	11/11 (100)	7/9 (77.8)	4/6 (66.7)	90/100 (90.0)		
Peak systolic velocity (cm/s)	10.15 (4.47–16.78)	8.53 (4.3–12.92)	19.81 (13.76–30.85)	12.1 (8.25–14.61)	10.53 (5.23–15.12)	12.3 (6.21–16.34)		
Pulsatility index	0.35 (0.11–0.61)	0.18 (0.12–0.41)	0.62 (0.13–0.68)	0.51 (0.32–0.74)	0.53 (0.41–0.82)			
Resistance index	0.3 (0.12–0.47)	0.16 (0.1–0.32)	0.4 (0.1–0.73)	0.34 (0.17–0.41)	0.32 (0.25–0.69)			
Surface							0.011 (−0.048 to 0.07)	NS
Smooth	0/32	12/13 (92.3)	8/11 (72.7)	9/9 (100)	6/6 (100)	22/100 (22.0)		
Irregular	32/32 (100)	1/13 (7.7)	3/11 (27.3)	0/9	0/6	78/100 (78.0)		
Elasticity							0.008 (−0.038 to 0.054)	NS
Compressible	4/32 (12.5)	13/13 (100)	0/11	0/9	0/6	14/100 (14.0)		
Rigid	28/32 (87.5)	0/13	11/11 (100)	9/9 (100)	6/6 (100)	86/100 (86.0)		
Mobility							0.106 (0.055 to 0.157)	< 0.01
Mobile	7/32 (21.9)	12/13 (92.3)	2/11 (18.2)	3/9 (33.3)	2/6 (33.4)	4/100 (4.0)		
Semi-fixed	25/32 (78.1)	1/13 (7.7)	9/11 (81.8)	3/9 (33.3)	0/6	32/100 (32.0)		
Fixed	0/32	0/13	0/11	3/9 (33.3)	4/6 (66.6)	64/100 (64.0)		
Ovarian crescent sign present	0/32	0/13	11/11 (100)	0/9	6/6 (100)	2/100 (2.0)	−0.172 (−0.23 to −0.114)	< 0.01
Locularity (if applicable)							0.099 (0.005 to 0.193)	< 0.05
Number of locules (1–5; 6–10; > 10)	> 10	> 10	NA	NA	NA	1–5		
Irregular size of locules	21/21 (100)	13/13 (100.0)	NA	NA	NA	26/26 (100)		
Septa (if applicable)							0.035 (−0.029 to 0.099)	NS
Width (mm)	3 (1–3)	3 (1–4)	NA	NA	NA	3 (2–5)		
Regular width of septa	19/19 (100)	13/13 (100.0)	NA	NA	NA	26/26 (100)		
Subjective assessment of flow (1–4)[11]	2	3	NA	NA	NA	3 (3)		
Involvement of uterus	0/32	0/13	0/11	0/9	0/6	18/100 (18.0)	0.060 (0.005 to 0.115)	< 0.05
Carcinomatosis‡	2/32 (6.3)	4/13 (30.8)	0/11	4/9 (44.4)	6/6 (100)**	44/100 (44.0)	0.041 (−0.008 to 0.09)	NS
Ascites‡	2/32 (6.3)	4/13 (30.8)	0/11	4/9 (44.4)	6/6 (100)	44/100 (44.0)	0.040 (−0.028 to 0.108)	NS
Parenchymal metastases	6/32 (18.8%) (liver)	6/13 (46.2) (liver)	0/11	0/9	5/6 (83.3) (liver)	4/100 (4.0) (liver)	−0.164 (−0.254 to −0.074)	< 0.01
Necrosis present in solid component	29/32 (90.6) (in up to 50% of solid component)	0/13	0/11	5/9 (55.6)	0/6	13/100 (13.0)	−0.222 (−0.272 to −0.172)	< 0.01

Characteristics data are given as *n*, *n* (%) or median (range). *Parametric testing by Hotelling's distribution model (a modification of Student's model), comparing all variables for metastatic vs primary tumors. †Gallbladder, bile duct and pancreatic cancer. ‡In all cases, ascites and carcinomatosis were present concurrently. §Eight (88.9%) Krukenberg tumors were smaller than 8 cm in diameter. ¶Only two tumors evaluated. **Four without pelvic tumor. max., maximum; NS, not significant.

Table 4 Differences between individual most common metastatic non-gynecological tumors and epithelial ovarian cancer as evaluated by multivariate regression derived from the OPLS model for selected individual variables

	Dependent variable									
	Colorectal cancer		*Upper gastrointestinal cancer*		*Lymphoma*		*Krukenberg tumor*		*Breast cancer*	
Independent variable	*Parameter (95% CI)*	P	*Parameter (95% CI)*	P	*Parameter (95% CI)*	P	*Parameter (95% CI)*	P	*Parameter (95% CI)*	P
Laterality	−0.123 (−0.206 to −0.04)	*	0.058 (−0.059 to 0.175)		0.242 (0.117 to 0.367)	**	−0.114 (−0.195 to −0.033)	*	−0.065 (−0.248 to 0.118)	
Distribution	−0.051 (−0.098 to −0.004)	*	0.147 (0.079 to 0.215)	**	0.021 (−0.048 to 0.09)		−0.044 (−0.143 to 0.055)		0.079 (−0.001 to 0.159)	
Structure	0.120 (0.057 to 0.183)	**	0.153 (0.036 to 0.27)	*	−0.080 (−0.116 to −0.044)	**	−0.250 (−0.32 to −0.18)	**	−0.098 (−0.185 to −0.011)	*
Papillary projections	0.071 (0.02 to 0.122)	*	−0.049 (−0.149 to 0.051)		−0.064 (−0.162 to 0.034)		−0.079 (−0.167 to 0.009)		−0.053 (−0.214 to 0.108)	
Echogenicity	0.002 (−0.083 to 0.087)		0.197 (0.128 to 0.266)	**	0.174 (0.119 to 0.229)	**	0.141 (0.032 to 0.25)	*	−0.102 (−0.176 to −0.028)	*
Homogeneity	−0.031 (−0.096 to 0.034)		−0.214 (−0.328 to −0.1)	**	−0.188 (−0.248 to −0.128)	**	−0.085 (−0.193 to 0.023)		0.236 (0.152 to 0.32)	**
Vascularity†	0.073 (−0.016 to 0.162)		0.011 (−0.066 to 0.088)		0.071 (−0.062 to 0.204)		0.117 (0.032 to 0.202)	*	0.102 (0.022 to 0.182)	*
Surface	0.333 (0.278 to 0.388)	**	−0.154 (−0.248 to −0.06)	**	−0.102 (−0.242 to 0.038)		−0.421 (−0.524 to −0.318)	**	0.015 (−0.049 to 0.079)	
Elasticity	0.058 (0.002 to 0.114)	*	−0.321 (−0.415 to −0.227)	**	0.057 (0.001 to 0.113)	*	0.095 (0.017 to 0.173)	*	0.064 (−0.006 to 0.134)	
Mobility	−0.092 (−0.156 to −0.028)	*	−0.169 (−0.21 to −0.128)	**	0.117 (0.015 to 0.219)	*	−0.040 (−0.144 to 0.064)		0.075 (0.017 to 0.133)	*
Ovarian crescent sign	−0.099 (−0.181 to −0.017)	*	−0.145 (−0.255 to −0.035)	*	0.361 (0.322 to 0.4)	**	−0.143 (−0.221 to −0.065)	**	0.409 (0.263 to 0.555)	**
Involvement of uterus	−0.075 (−0.139 to −0.011)	*	0.119 (0.024 to 0.214)	*	0.036 (−0.06 to 0.132)		−0.085 (−0.14 to −0.03)	*	−0.236 (−0.345 to −0.127)	**
Carcinomatosis	−0.102 (−0.141 to −0.063)	**	−0.003 (−0.127 to 0.121)		−0.102 (−0.17 to −0.034)	*	0.167 (0.066 to 0.268)	**	0.180 (0.103 to 0.257)	**
Ascites	−0.154 (−0.204 to −0.104)	**	0.104 (0.033 to 0.175)	*	−0.026 (−0.059 to 0.007)		0.126 (0.059 to 0.193)	**	−0.038 (−0.186 to 0.11)	
Parenchymal metastases	0.141 (0.066 to 0.216)	**	0.052 (−0.019 to 0.123)		−0.067 (−0.18 to 0.046)		−0.042 (−0.118 to 0.034)		0.386 (0.247 to 0.525)	**
Necrosis‡	0.444 (0.329 to 0.559)	**	−0.258 (−0.445 to −0.071)	*	−0.223 (−0.341 to −0.105)	**	0.144 (−0.025 to 0.313)		0.136 (0.063 to 0.209)	**
Size	0.090 (0.036 to 0.144)	**	0.079 (0.003 to 0.155)	*	0.108 (−0.014 to 0.23)		−0.187 (−0.345 to −0.029)	*	0.066 (−0.074 to 0.206)	
R^2	69.7% (67.1%)		63.2% (60.0%)		53.2% (48.5%)		37.9% (32.7%)		49.2% (43.8%)	

Values in the table represent regression coefficients in multivariate regression model for individual dependent variables. R^2 gives percentage variation among individual dependent variables.
*$P < 0.05$. **$P < 0.01$. †Subjective assessment. ‡As suspected based on ultrasound.

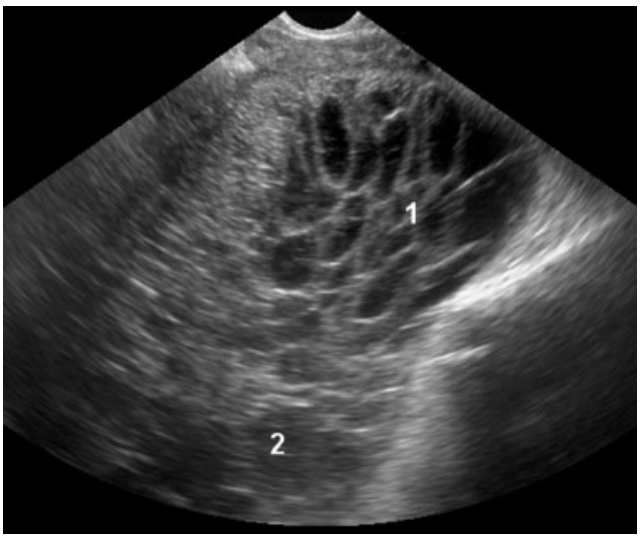

Figure 3 Metastasis of upper gastrointestinal tract tumors (gallbladder, bile ducts, pancreas): multilocular-solid tumor with small multiple locules (1) and solid portion (2).

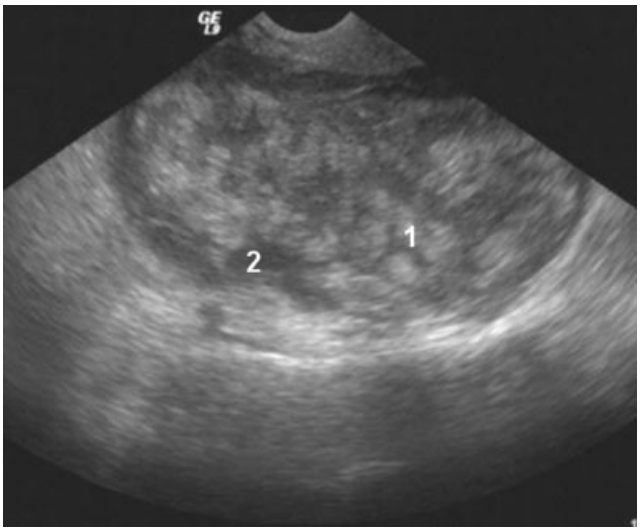

Figure 4 Metastasis of lymphoma: well-defined heterogeneous tumor with multiple hyperechogenic areas (1) and distinct hypoechogenic border (2).

these variables distinguished between metastatic non-gynecological tumors and epithelial ovarian cancer with a sensitivity of 81.8% and specificity of 98.8%.

Krukenberg tumor (metastatic gastric cancer only)

Krukenberg tumors were typically ovarian tumors of heterogeneous structure, with mostly isoechogenic with hypoechogenic areas, and with potential presence of necrosis (Figure 5) and bosselated but smooth surface. Krukenberg tumor vascularization (outside the area of potential necrosis) was assessed as having a score of 3. The typical feature of 'lead vessel'[10] was observed in one tumor only. However, the retrospective nature of the study, involving stored scan descriptions, meant that lead vessel sign assessment was not a standard part of the

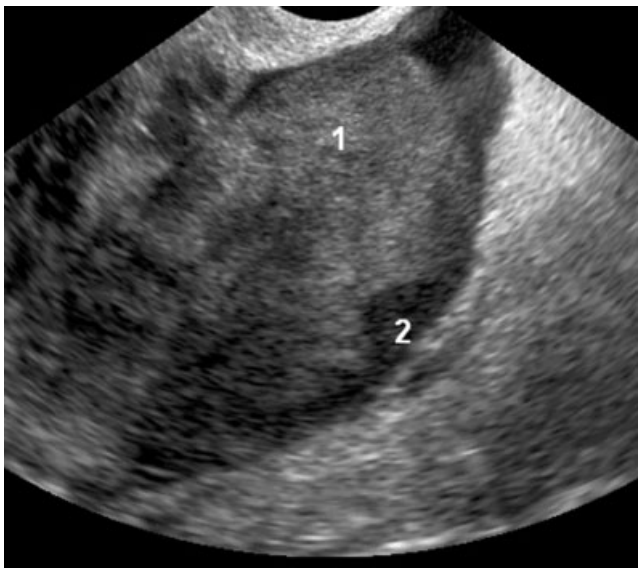

Figure 5 Krukenberg tumor (metastasis of gastric cancer): solid, bosselated but smooth, heterogeneous tumor, that is mostly isoechogenic with both hyperechogenic (1) and hypoechogenic (2) areas.

institutional protocol. Thus the low presence of this sign is not surprising.

Krukenberg tumors differed highly significantly ($P < 0.01$) from the primary ovarian cancer group in structure, surface, presence of ovarian crescent sign, presence of carcinomatosis and ascites (Table 4). However, in the prediction model these variables distinguished between metastatic non-gynecological tumors and epithelial ovarian cancer with low sensitivity (33.3%) and a specificity of 96.5%.

Breast cancer

Pelvic metastases derived from breast cancer were most commonly present as hyperechogenic carcinomatosis with ascites. In four of the six (66.7%), there was only carcinomatosis and no pelvic tumor. Carcinomatosis foci were hyperechogenic (contrary to the carcinomatosis foci of primary epithelial ovarian cancer) (Figure 6). In 5/6 tumors (83.3%), both carcinomatosis above the level of the pelvis and parenchymal metastases were found.

These tumors differed highly significantly ($P < 0.01$) from the primary ovarian cancer group in homogeneity, presence of ovarian crescent sign, involvement of uterus, presence of carcinomatosis, parenchymal metastases and presence of possible necrosis (Table 4). In the prediction model these variables distinguished between metastatic non-gynecological tumors and epithelial ovarian cancer with a sensitivity of 83.3% and a specificity of 99.4%.

Others

The remaining tumors constituted a heterogeneous group of metastases manifesting different biological behavior and primary tissues, each type being detected in fewer than five cases in our study group.

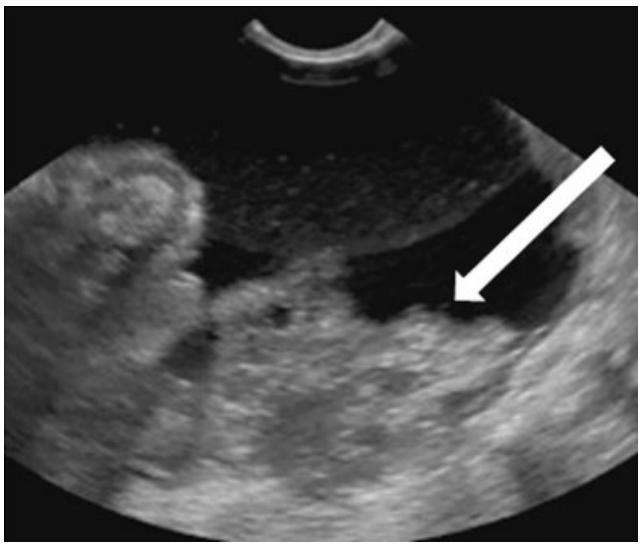

Figure 6 Metastasis of breast cancer: hyperechogenic carcinomatosis in the pelvis (arrow).

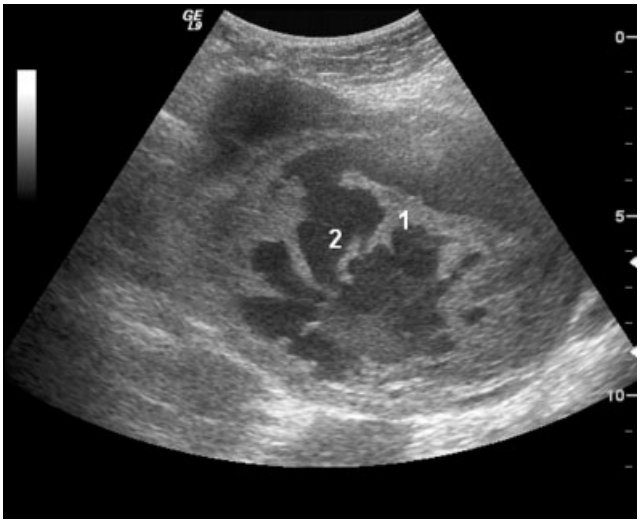

Figure 7 Metastasis of gastrointestinal stromal tumor: well-defined tumor (with distinct border) with multiple hyperechogenic incomplete septa (1) and hypoechogenic content (2).

Gastrointestinal stromal tumor was observed in four (4.3%) patients. Tumor size ranged from 7 to 10 cm. All tumors were located intraperitoneally. In half of the cases, the tumor was ovarian, in each case being unilateral. In all cases the structure was multilocular-solid with hyperechogenic septa, hypoechogenic necrotic areas and anechogenic content of locules. Septa were often incomplete and richly vascularized (score, 3). The width of septa and pseudosepta ranged from 5 to 10 mm and was irregular within the septa (Figure 7).

Pelvic metastases from urinary bladder cancer were found in three (3.3%) patients. Tumor size ranged from 5 to 10 cm. All tumors were intraperitoneal, extraovarian and unilateral, with a multilocular-solid structure and strongly heterogeneous septa. The number of locules was always less than 10, the width of the septa was distinctly irregular, with necrotic areas and blurred borders (Figure 8). The solid component was distinctly necrotic with rich peripheral vascularization.

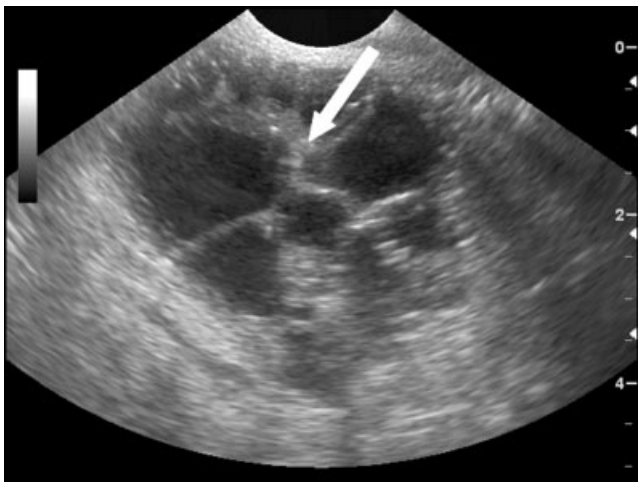

Figure 8 Metastasis of urinary bladder cancer: tumor with blurred border, with hyperechogenic septa of irregular width (arrow).

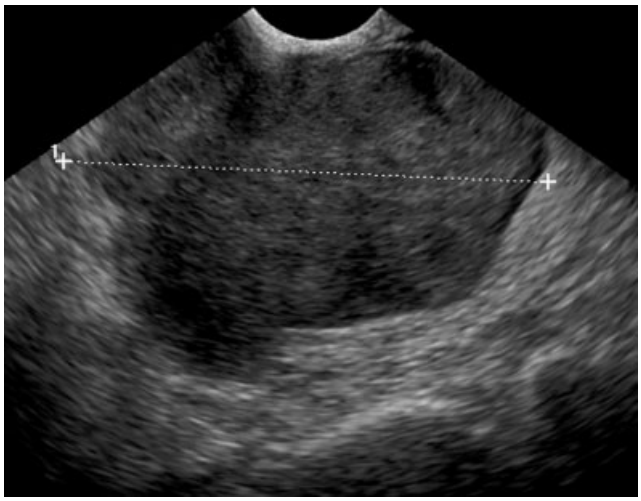

Figure 9 Metastasis of neuroendocrine tumor: solid heterogeneous, mostly hypoechogenic tumor (calipers).

Metastases derived from neuroendocrine tumors were seen in two (2.2%) patients. The tumors were 8 and 10 cm in size. Both tumors were intraperitoneal, unilateral and ovarian. The structure was solid, heterogeneous and mostly hypoechogenic (Figure 9). Vascularization was scored as 2 in both cases. The tumors had blurred borders and were mobile. In both patients, hypoechogenic liver metastases were present; there was no carcinomatosis or ascites.

In two (2.2%) patients carcinoid metastases were observed. The tumors were 3 and 5 cm in size. Both tumors were unilateral and ovarian. They were solid heterogeneous tumors with multiple small hyperechogenic foci (Figure 10). Subjective assessment of vascularization assigned both a score of 3.

The remaining tumors occurred in only one case each (Table 2) thus their sonographic parameters could not be analyzed systematically.

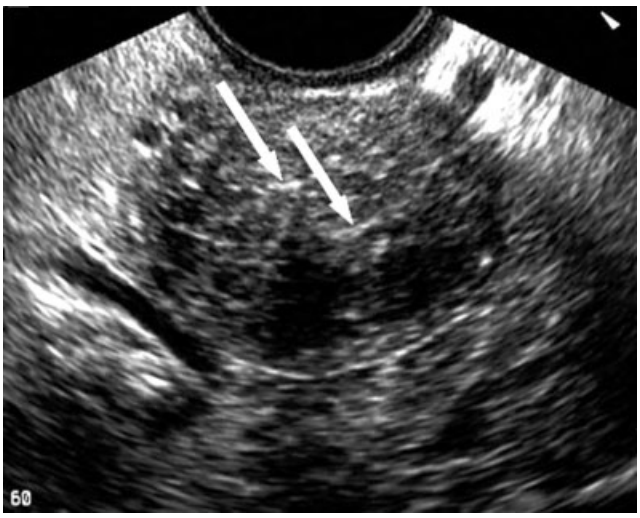

Figure 10 Carcinoid metastasis: well-defined (with sharp border) solid tumor, with heterogeneous structure and hyperechogenic foci (arrows).

DISCUSSION

We have described the sonographic characteristics of the most common extragenital tumors detected in the pelvis (as ovarian metastases or metastases outside the ovaries) in our study population. We assessed individual ultrasound characteristics in specific types of tumor and defined the sonographic characteristics common to non-gynecological pelvic masses compared with epithelial ovarian cancer.

The most frequent non-gynecological tumors in the pelvis were metastases derived from colorectal cancer, followed by those derived from upper gastrointestinal tract cancer (gallbladder, bile ducts, pancreas), non-Hodgkin lymphoma and Krukenberg tumor. The spectrum of non-gynecological tumors in our study differs from that in published retrospective studies investigating pathological[4,12] and ultrasonographic[5] findings, with the most frequently found non-gynecological tumor in these studies being colorectal cancer followed by breast cancer and Krukenberg tumor. Especially striking was the significant representation of lymphomas, which occurred only in individual cases in the other study populations. Our study, however, was not limited to metastases of the ovaries alone, but covered all pelvic masses, i.e. also those located outside the ovaries, since in practice it may be challenging to discriminate between an ovarian and a non-ovarian tumor location; we believe that this approach better represents the clinical situation. The spectrum of tumors apparently reflects a certain similarity of their structure to gynecologic tumors (the structure of mucinous upper gastrointestinal tract tumors is similar to that of mucinous ovarian tumors) since the patients with such tumors are most likely to be referred to a gynecologist.

Sonomorphology of non-gynecological pelvic masses correlates well with their known pathological description[13]. Our study, though, revealed a much lower frequency (13.0%) of bilateral pelvic/ovarian pathology than that reported in the literature (67–75%)[14]. The lower occurrence of bilateral tumors is also obvious if one considers only the ovarian metastatic tumors (6/39, 15.4%). This might be due to the different spectrum of tumors in our study, which included not only ovarian but all pelvic tumors. In addition, only 42% of the patients underwent surgery, so that, in the majority of cases, the uni/bilaterality was not proved histologically.

Discrimination between primary ovarian cancer and a non-gynecological tumor is of particular importance for clinical practice since their management may differ considerably. Suspicion of a tumor of non-gynecological origin should be articulated before the eventual surgical intervention. Even though metastatic pelvic masses form a heterogeneous group, certain ultrasound characteristics can be defined which distinguish them from primary ovarian cancer.

In our study no purely cystic (unilocular or multilocular) tumor was observed, a solid portion being present in all tumors. A purely solid structure was detected in half of the tumors, while in the remaining cases a cystic part was seen also. While the majority of studies that were focused on morphologic differences between primary ovarian and non-ovarian pelvic masses[15–18] show that a non-gynecologic pelvic mass is most commonly purely solid, our study did not find evidence to support this. The presence of a cystic component thus does not rule out non-gynecological tumor. Therefore, not only is it essential to asses tumor structure, it is also necessary to consider its inner morphology, with special attention being paid to the potential primary origin of metastatic tumors[5].

A feature indicative of metastatic tumors, with high statistical significance ($P < 0.01$), was the combination of sonomorphologic and Doppler findings indicating possible presence of necrosis, typical primarily of colorectal cancer metastases, metastases of some upper gastrointestinal tract cancers (gallbladder, bile ducts, pancreas) and Krukenberg tumor. However, ultrasound can only suspect the presence of necrosis, not confirm the histological diagnosis. Larger prospective studies focused on correlation of histology and ultrasound findings regarding necrosis should clarify the usability of these parameters in standard scan protocols.

Liver metastases are relatively uncommon in primary ovarian cancer[19,20]; in our group of non-gynecological pelvic metastatic tumors, metastases in the liver were detected in one third (33.96%) of patients by means of transabdominal ultrasound examination. Thus the morphological assessment of pelvic mass together with the presence of parenchymatous liver metastases may be a reason to search for a primary site of the tumor other than the ovary. Transabdominal ultrasound examination thus becomes an integral part of the examination schedule.

Doppler sonography does not allow discrimination between non-gynecological and gynecological tumors. However, it is an important factor in determining the nature (benign vs. malign) of detected lesions[7]. Also, in combination with B-mode imaging, it facilitates the suspicion of necrosis and detection of the borders of the lesion with the surrounding structures in cases in which

this border is not well recognized on B-mode imaging (when the tumor is isoechogenic to the surrounding structures).

A knowledge of the specific ultrasound characteristics of non-gynecological tumors can change the focus of diagnostic efforts in cases of tumors in which pelvic metastases are merely the first sign of a tumor with the primary site being somewhere other than the internal genitalia. The sonomorphology of such metastatic tumors may facilitate the identification of the primary tumor and help determine the optimum management for the patient.

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