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US, CT and MR as Diagnostic Implements in The Detection of Various Primary Malignant Diseases and Ovarian Metatastases Coming from Different Sites of Primary Origin of The Tumor: A Review

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Abstract

Object: *We propose a literature review of ultrasound, computer tomography and magnetic resonance in the differention of ovarian lymphoma and metatstatic neoplasm to ovaries correlate with imagies and tables.*

Methods: *Review of the literature.*

Introduction: *Imaging techniques play a fundamental role in the non-invasive evaluation of patients with extranodal lymphoma, both for initial staging and during follow-up and in monitoring the response to treatment. In radiodiagnostics, the means most used in patients with lymphoma are ultrasound, CT, MR and hybrid PET/CT.*

Dissussion: *Unfortunately, in modern literature there are few sources that highlight the major differences that can be detected by ultrasound, CT and MR between the various primary ovarian malignant diseases and ovarian metastases coming from different sites of primary origin of the tumor. In my work I analyze some of them with figures and tables.*

Conclusion: *We would underline that the radiological images of a secondary ovarian neoplasm differ from a ovarian lymphoma based on the nature of the primary disease.*

Introduction

The imaging techniques most used in the diagnosis of ovarian neoplasms, whether lymphomas or other types of tumors, are represented primarily by ultrasound, followed by CT and MR. In odiern literature there are small sources that highlight the major differences that can be detected by ultrasound between the various primary ovarian malignant diseases and ovarian metastases coming from different sites of primary origin of the tumor. In our work we analyze some of them.

It is important to focus on the description of these rare but fundamental sources, given that as we have already specified previously, the diagnosis of lymphoma initially makes use of imaging techniques which must be as punctual and accurate as possible.

For this reason, given that lymphoma often enters into a differential diagnosis with other types of primary ovarian tumors or with metastatic forms, we will now describe the various differences found by the authors in their retrospective studies between these different ovarian malignant forms, through use of ultrasound.

Discussion

Clinical and sonographic figures of uncommon malignant tumors of the ovary

Alcazar et al. (2011), in May 2011 published a very interesting and unique article, given that there are no comparative studies in the literature between the various clinical and sonographic figures of uncommon ovarian malignancies.

The study by these authors is retrospective, with the analysis of 98 masses in 89 patients, whose diagnosis was ovarian malignancy. The objective is to define the ultrasound images in the gray scale and the Color-Doppler score of these masses. All patients underwent transvaginal ultrasound and the ultrasound figures stopped to analyze:

1. Laterality;
2. Presence of ascites;
3. Tumor volume;
4. Morphological characteristics (unilocular, multilocular, solid-unilocular, solid-multilocular and solid);

5. Color Doppler score (subjective evaluation of the blood flow value as: absent, poor, moderate or abundant).

Table 1 shows the various histological types of malignant tumors present in the population examined.

Undifferentiated carcinoma	20	20
Clear-cellcarcinoma	16	16,3
Transitional-cell carcinoma	15	15,3
Epidermoid carcinoma	3	3
Malignant adenofibroma	2	2
Mixed miillerian tumor	2	2
Oat-cell carcinoma	1	1
Immature teratoma	5	5
Dysgerminoma	2	2
Endoderma! sinus tumor	1	1
Malignant struma ovarii	1	1
Choriocarcinoma	1	1
Malignant granulosa cell tumor	8	8,2
Sertoli-Leydig tumor	2	2
Sclerosing tumor	1	1
Carcinosarcoma	4	4
Fibrosarcoma	3	3
Liposarcoma	1	1
Sarcoma	1	1
Lymphoma	9	9
Total	98	100

Table 1 (Alcazar et al., 2011)
Histopathological diagnosis of 98 ovarian neoplasms in 89 women.

Many ovarian neoplasms are tumors originating from the surface of the ovary. (Valentin et al., 2006) show how common epithelial, serous, mucinous and endometrial neoplasms are generally unilocular or multilocular cystic-solid masses with abundant vascularization.

The presence of ascites and bilaterality are frequently observed especially in advanced stage tumors.

Ovarian tumors are considered rare or uncommon with a prevalence of 5% compared to all forms of ovarian tumors and are grouped according to their histology in accordance with the WHO classification. Specific data regarding the ultrasound findings of these tumors are scarce in the literature.

In the analysis, clear cell ovarian carcinoma appears as a cystic-solid mass with abundant vascularity in both pre-menopausal and post-menopausal women (Fig. 1). Ascites and bilaterality are uncommon in this type of neoplasm.

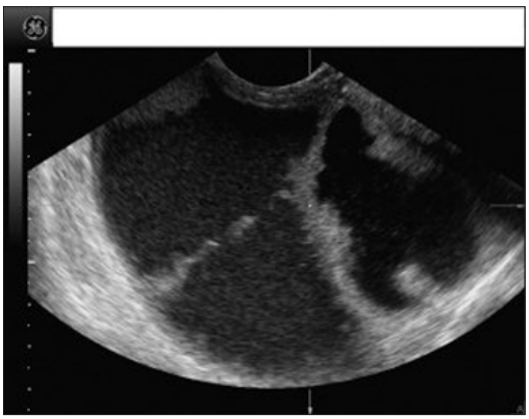

Figure 1 (Valentin et al., 2006)
[Transvaginal ultrasound of clear cell ovarian cancer showing a cystic mass with dense irregular septa and irregularities in the inner surface of the wall.]

However, undifferentiated cell carcinoma and transitional cell carcinoma (belonging to the category of ovarian epithelial neoplasms, such as clear cell carcinoma) appear in this series as purely solid, with abundant vascularization in post-menopausal women, and bilaterality and ascites are usually present.

Regarding other rare epithelial tumors such as epidermoid or mullerian cell carcinoma, the data obtained are in agreement with those reported in previous articles by (Emoto et al., 2000) and (Dos Santos et al., 2007) who describe them as large and apparently cystic masses with solid components and poor vascularization within the solid component.

In general in the case series of (Valentin et al., 2006), germ cell tumors appear as unilateral solid masses with abundant vascularization in young women (Fig.2). In these patients CA-125 tends to be high and ascites and bilaterality are normally absent.

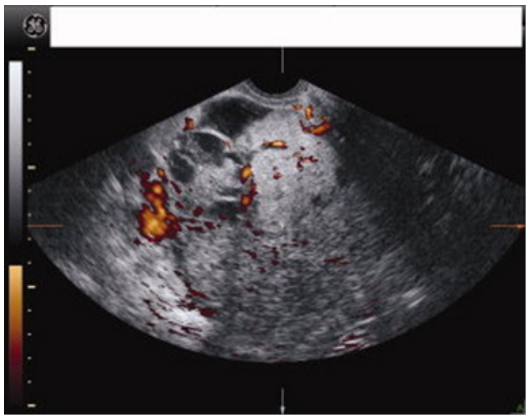

Figure 2 (Valentin et al., 2006)
[Germ cell tumor. Color-Doppler ultrasound Transvaginal showing a solid mass with irregular contours, moderate vascularity with presence of central vessels.]

Stromal line tumors generally appear unilateral with small solid masses in perimenopausal women. (Fig.3).

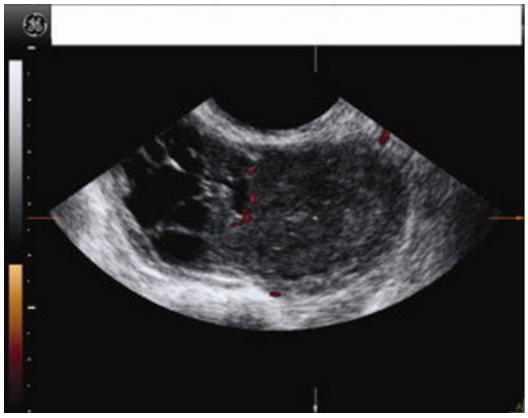

Figure 3 (Valentin et al., 2006)
[Ovarian tumor of the stromal line (malignant with granulosa cells). Transvaginal ultrasound shows a solid tumor with a cystic component.]

Other authors such as (Demidov et al., 2008), (Kim et al., 2010) and (Van Holsbeke et al., 2008) also report the same results observing that ovarian tumors of the stromal line appear purely solid. Ascites and bilaterality are uncommon, and vascularity is poor or absent. CA-125 is normal in many cases.

As for sarcomas, they generally appear as large and solid masses, unilateral with moderate or abundant vascularization, CA-125 is moderately elevated.

The primary ovarian lymphoma also appears solid with moderate/high vascularity and in the nine cases observed, eight appear unilateral. Ascites is absent and CA-125 is within normal levels in most cases. (Crawshaw et al., 2007) and (Yamada et al., 2003) report similar results. On the other hand, many articles report cases of ovarian lymphoma that mimics cancer also due to the elevation of CA-125.(Allen et al., 2004; Anand et al., 2011; Arnogiannaki et al., 2011; Kapetanakis et al., 2010; Snijders et al., 2010; Nanda et al., 2009; Pectasides et al., 2008).

Comparative ultrasound study of ovarian metastases originating from different types of primary tumors

In the literature, as we have already seen previously, there are rare sources that accurately describe the sonographic images obtained from the study of malignant ovarian tumors. (Zhao et al., 2011; Ozat et al., 2011) Likewise, there are only two articles present which highlight, through a retrospective study, the different ultrasound images of ovarian metastases in relation to the primary tumor from which they originate.

The most recent study was carried out by (Guerriero et al., 2011), in October 2011. This article often compares their results with those of the only previously carried out study dealing with this specific topic, written by Testa et al in 2007. (Testa et al., 2007).

The authors aim to describe how ovarian metastases appear in accordance with the origin of the primary tumor, in ultrasound and color Doppler images, also in relation to biochemical and clinical parameters.

The study is a retrospective analysis of 116 masses in 92 patients (average age: 51 years), evaluated and treated in three different European university centers. All patients underwent a transvaginal Eco-Color-Doppler before surgery and tumor removal. Women in their 50s with amenorrhea present for more than 12 months were considered to be in a premenopausal state.

The sonographic examination was performed using different ultrasound machines during the study periods. The gray scale morphological evaluation of the ovarian masses was performed by observing some parameters:

1. bilaterality;
2. septa;
3. echogenicity;
4. papillary projections or solid areas.

According to these parameters, the tumor was classified as unilocular cystic, multilocular cystic, unilocular solid-cystic, multilocular solid-cystic or solid.

After the morphological evaluation, Color Doppler examination was carried out to identify the vascularization within the mass, classifying the flow as absent, poor, moderate or abundant.

On the same day of the ultrasound examination, the value of the tumor marker CA-125 is analyzed via blood sampling. Subsequently, all tumor masses were removed and a histological diagnosis was obtained.

The variables were evaluated as follows:

1. Clinic: age of patients and menopause
2. Laboratory: CA-125 expressed in IU/mL
3. Ultrasound characteristics
4. Bilaterality
5. Grayscale
6. Color-Doppler Score
7. Tumor volume
8. Histological diagnosis

The results of this study highlight that 24 patients (26%) have a bilateral tumor on ultrasound. Therefore the total number of tumors evaluated is 116. Histological diagnoses are provided in Table 2.

	N	%
Stomach	28	24.1%
Colorectal	32	27.6%
Breast	20	17.2%
Uterine*	17	14.7%
Lymphoma	4	3.4%
Liver-Pancreas-Biliary tract**	4	3.4%
Miscellaneous***	11	9.5%
Total	116	100.0%

Table 2 (Testa et al., 2007)

Histological diagnosis of different types of metastatic tumors in relation to the origin of the primary tumor.

There are no significant differences in age, menopausal status and CA-125 marker values. Bilaterality appears more frequent in metastatic tumors originating from the stomach (55.6%) and is never present in the four cases of lymphoma nor in metastases originating from the biliary-hepato-pancreatic tract.

The mean tumor volume is significantly low in breast metastases (33.5mL) compared to metastases from the stomach, colorectal and miscellaneous group tumors. of the 116 masses, 75 (64.7%) are purely solid, 6 (5.2%) are unilocular solid, and 35 (30.2%) are multilocular solid. On B-mode ultrasound, solid tumors are much more frequent in breast metastases (95%) (Fig.4) when compared with those of the stomach, colorectal (Fig.5), and uterus.

No further differences were highlighted between other groups. Many tumors could be moderately or highly vascularized (Fig. 6-7) but there were no statistical differences in color scale between the various types of metastatic tumors.

Figure 4 (Testa et al., 2007)
[Typical ultrasound image of the solidity of ovarian metastases from breast cancer.]

Figure 5 (Testa et al., 2007)
[Image of ovarian metastases from a colorectal carcinoma with solid-multilocular component.]

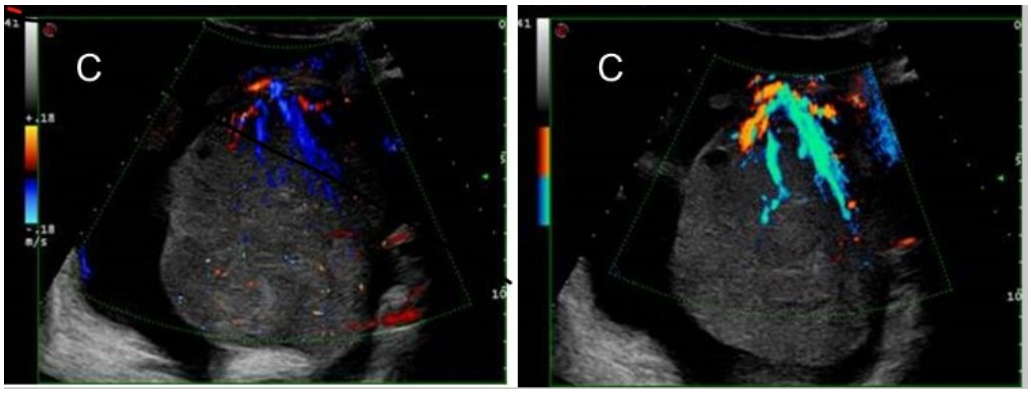

Figure 6 (Donatello et al., 2023)
[TV Color and Power Doppler TVS clearly depict the main vessel (the "lead vessel") entering from the periphery to the center of the ovarian mass, with many branching vessels of thinner width. (White arrow: ovarian follicle).]Donatello D 2023

Figure 7 (Testa et al., 2007)
[Color-Doppler ultrasound. The image shows the vascularity of ovarian metastases from colon cancer.]

The authors, after having highlighted these characteristics and reported them in specific tables, in their discussion compared the results obtaine with the study published in 2007 that analyzes the same topic.

Precisely for this reason they compare, as Testa did in his article(Testa et al., 2007), metastases originating from the stomach, breast, lymphoma and uterus, with metastases deriving from tumors of the colorectal, appendix and biliary tract.

From that data emerges that the authors of the two studies are in agreement above all on the similarity of ovarian metastases coming from the stomach, breast and lymphoma, given that they appear solid and smaller than colorectal metastases.

On the other hand, (Guerriero et al., 2011) highlights the importance of ultrasonography in identifying ovarian metastases in patients with previous breast cancer, given that they appear much smaller. but still solid, compared to all other types of metastatic tumors.

Unlike Testa (Testa et al., 2007), in Guerriero's study no significant differences are highlighted in the color score highlighted by Eco-Color -Doppler.

Table 10 shows the sonographic morphology in relation to the type of primary tumor of origin in the series of 67 women affected by metastatic ovarian cancer, analyzed in Testa's study, where the abundant vascularization of the ovarian metastases from lymphoma is observed, with a Color score equal to 4, in all three types of ovarian metastatic lymphomatous involvement. (Testa et al., 2007).

Testa also describes in an article published in 2008 the sonographic images of the vascularization in solid ovarian metastases. It highlights the appearance of the so-called lead vessels, represented by major vessels that are located on the periphery of the mass and penetrate inside the latter, emerging into an arborization of minor vessels. (Testa et al., 2007; Testa et al., 2008; Koyama et al., 2007; Liu et al., 2007; Brown et al., 2001; Dalloul et al., 2007; Gregorio et al., 2009; Gligorievski et al., 2018; Crawshaw et al., 2007; Yamada et al., 2003; Donatello et al., 2023) From his study it appears that this vascularization characteristic is present in 11/31 cases of ovarian metastases, while it is present in only 0.01% of primary ovarian tumors. (Testa et al., 2008; Koyama et al., 2007; Liu et al., 2007; Brown et al., 2001; Dalloul et al., 2007; Gregorio et al., 2009; Gligorievski et al., 2018; Crawshaw et al., 2007; Yamada et al., 2003; Donatello et al., 2023).

	Colon/ rectum/ appendix	*Biliary tract*	*Stomach*	*Lymphoma*	*Breast*	*Uterus*	*Pancreas*
Number of patients	17	5	15	3	10	13	4
Locularity (*n* (%))							
Unilocular	1 (5.5)	—	—	—	—	—	—
Unilocular-solid	1 (5.5)	—	—	—	—	—	1 (25)
Multilocular	4 (24)	3 (60)	—	—	1	—	—
Multilocular-solid	8 (47)	1 (20)	—	—	—	2 (15)	1 (25)
Solid	3 (18)	1 (20)	15 (100)	3 (100)	9 (90)	11 (85)	2 (50)
Diameter (mm, median (range))	113 (16–179)	150 (55–200)	84 (43–170)	120 (73–130)	55 (27–98)	82 (28–220)	89 (44–149)
Irregular borders (*n* (%))	15 (88)	4 (80)	7 (47)	1 (33)	5 (50)	6 (46)	4 (100)
Echogenicity (*n* (%))							
Anechoic	4 (24)	1 (20)	2 (13)	—	1(10)	2 (15)	2 (50)
Low level	8 (47)	3 (60)	1 (7)	—	—	1 (8)	—
Ground glass	—	—	—	—	—	1 (8)	—
Hemorrhagic	1 (6)	—	—	—	—	—	—
Mixed	2 (11.5)	—	—	—	—	2 (15)	1 (25)
No cystic fluid	2 (11.5)	1 (20)	12 (80)	3 (100)	9 (90)	7 (54)	1 (25)
Papillary projections (*n* (%))	6 (35)	0	0	0	0	2 (15)	0
Color score (*n* (%))							
1	1 (6)	—	—	—	—	—	2 (50)
2	4 (24)	3 (60)	2 (13)	—	2 (20)	1 (8)	—
3	7 (41)	2 (40)	8 (54)	—	4 (40)	6 (46)	1 (25)
4	5 (29)	—	5 (33)	3 (100)	4 (43)	6 (46)	1 (25)

Table 3 (Testa et al., 2008)
Sonographic morphology according to the type of primary tumor in a series of 67 women affected by metastatic ovarian cancer.

Testa highlights the multilocularity of the masses derived from colorectal or appendicular metastases, while in the warrior study the multilocular-solid masses are not more numerous than the solid ones. (Testa et al., 2007).

We also observe in the ultrasound scan below the similarity between the metastases coming from a breast cancer and from a disseminated lymphoma, with the metastases coming from a gastric tumor (Krukenberg's tumor). (Testa et al., 2007; Testa et al., 2008; Koyama et al., 2007; Liu et al., 2007; Brown et al., 2001; Dalloul et al., 2007; Gregorio et al., 2009; Gligorievski et al., 2018; Crawshaw et al., 2007; Yamada et al., 2003; Donatello et al., 2023).

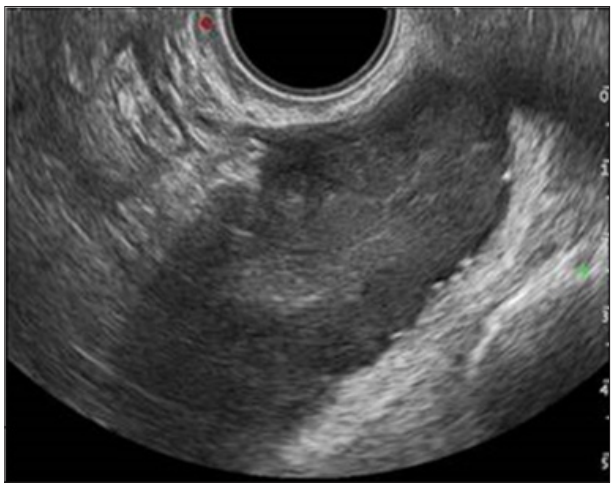

Figure 8 [Donatello et al., 2023]
TV ultrasonography shows an increase in size of the left ovary transformed into a mobile solid tumefaction, with well-defined external contours, and preserved cleavage planes, vascularized on Power Doppler (color-score 2)These findings appear suggestive of an ovarian localization of the underlying hematologic disease; the hypothesis of secondary involvement by intra-peritoneal dissemination of neoplastic cells from gastric K (Krukemberg) is likely.

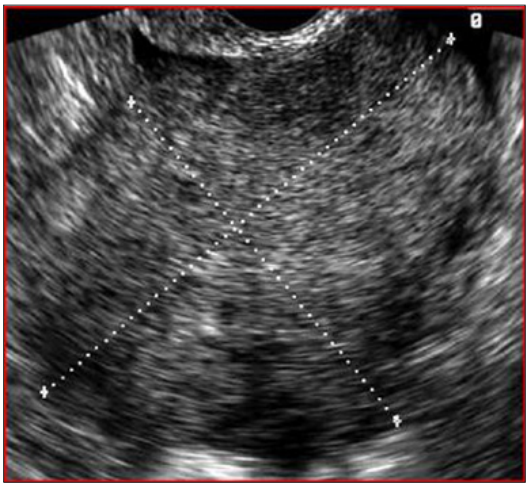

Figure 9 (Testa et al., 2007)
[Ovarian ultrasound showing a metastatic mass derived from breast cancer.]

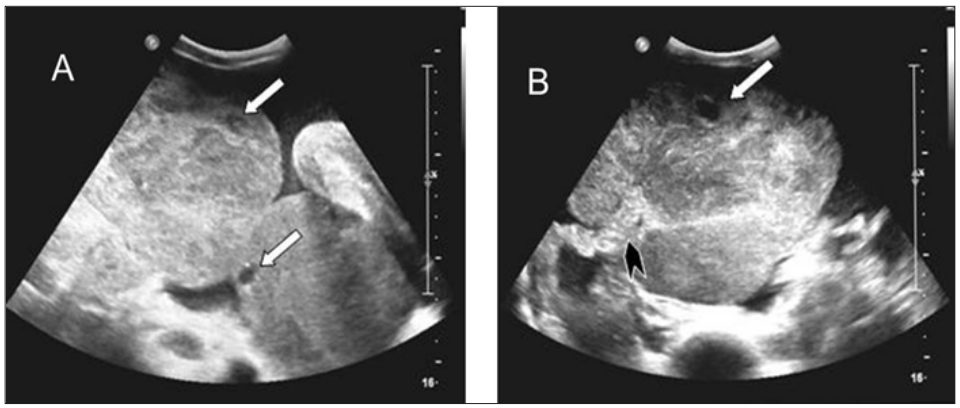

Figure 10 (Donatello et al., 2023) A 44 years old woman with occult NHL (Burkitt type) presenting with abdominal pain and distension, and bilateral solid ovarian masses (same patient as Fig.1). Sovrapubic US shows small anechoic areas of cystic appearance lining at the periphery of the ovarian solid masses, indicative of preserved ovarian follicles (A, B). The vascular pedicle is clearly visible entering from the border to the core of the ovarian mass (B). (White arrow: ovarian follicle. Black arrowhead: vascular pedicle).

CT and MR as tools for the recognition of secondary ovarian involvement

Koyama et al. (2007), carried out a comparative study in 2007 between the various figures that appear in CT and MR, aimed at highlighting the morphological differences that exist between the various types of metastases that can affect the ovary.

In fact, we know that the ovary is a preferential site for metastases from other organs.

In our study it is essential to observe the radiographic images that may occur during secondary ovarian involvement by a lymphoma, i.e. metastases at the ovarian level originating from a primary neoplasm, represented by a lymphoma. The recognition of the radiological findings of secondary ovarian involvement is a benefit, both to highlight the origin of the metastases, and therefore outline the primary tumor, and to determine the correct treatment of patients based on the tumor of origin.

The most common primary origins of ovarian metastases are: colon, stomach, breast, genitourinary tract, and to a lesser extent, appendix, pancreas, biliary tract, and lungs. Accurate diagnosis of secondary ovarian cancer is crucial because misinterpretation can have serious adverse consequences for patients. In fact, let us remember that sometimes ovarian involvement represents the first manifestation of the disease.

Generally, one of the radiological features suggestive of metastatic neoplasia is bilaterality.

From the studies described above, however, we know that for example in ovarian lymphoma, there can be bilaterality whether it is primary or secondary. We also know that primary ovarian tumors such as endometrioid carcinoma or serous papillary adenocarcinoma are also frequently bilateral, so the figure of bilaterality should not be considered a certain parameter in the distinction between primary and secondary involvement.(Liu et al., 2007; Brown et al., 2001; Dalloul et al., 2007).

The analysis of all of this studies is very important, because the specialist should be able to differentiate a lymphoma that gives secondary involvement from other types of metastatic ovarian cancers, precisely because the treatment is very different.

In fact, we know that even disseminated lymphoma is treated with systemic chemotherapy, unlike the surgical treatments provided for other metastatic primary tumors.

Metastatic ovarian tumor from gastric carcinoma (Krukenberg)

The images of a Krukenberg tumor (gastric metastatic tumor) highlight that the masses are:

- Bilateral;
- Lobulated ;
- Solid.

On T2-weighted MR images, solid tumor components typically show low to high signal intensity. The tumor may occasionally present cystic areas. A blank signal may frequently be observed, probably representing more vascularized areas within the tumor. In higher contrast images in both CT and MR the masses demonstrate an increase in homogeneity (Fig. 11-12-13).(Gligorievski et al., 2018; Crawshaw et al., 2007; Yamada et al., 2003; Donatello et al., 2023).

Figure 11 (Gligorievski et al., 2018)
Hydro CT on the stomach. Expressed infiltration of the stomach wall, the same is thickened, rigid with reduced volume in the region of the corpus and antrum. The stomach loses its ability to distend. It is most often seen in diffuse adenocarcinoma of the stomach. There is a fluid collection or ascites around the liver and the spleen. Finding for the neo-infiltration process of the stomach of scirrhous type-linitis plastica, with metastases in the peritoneum. CT, computed tomography.

Figure 12 (Gligorievski et al., 2018)
CT of the abdomen and pelvis. Two large soft tissue tumor formations that originate from the ovaries are seen in the pelvis and a free fluid is seen in the peritoneum. Tumor masses are with expressed and heterogeneous contrast enhancement. Finding for MS changes in the ovaries and peritoneum. CT, computed tomography.

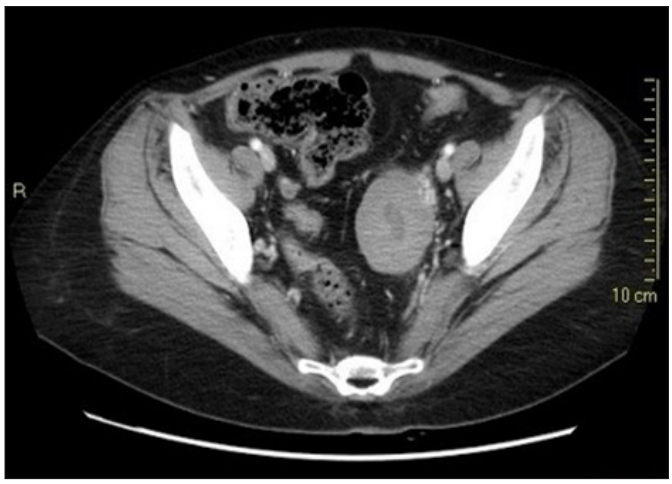

Figure 13 CT investigation performed for the staging of gastric adenocarcinoma, detected an oval expansive formation (maximum diameter 60x55x42 mm) with regular margins, modest contrast - enhancement and central hypodense area due to necrotic phenomena in the left adnexal site.

Metastatic Ovarian Tumor from Colorectal Carcinoma

Ovarian metastases from colorectal cancer can sometimes represent the first manifestation of this type of disorder. At the same time they are very frequent in patients aged around 40, with a total percentage of 18-27% compared to older women. Overall, metastases have heterogeneously high signal intensity on T2-weighted images, with areas of extensive necrosis. They are generally bilateral and cystic. The image below show us the characteristics of this type of secondary ovarian involvement (Fig. 14).

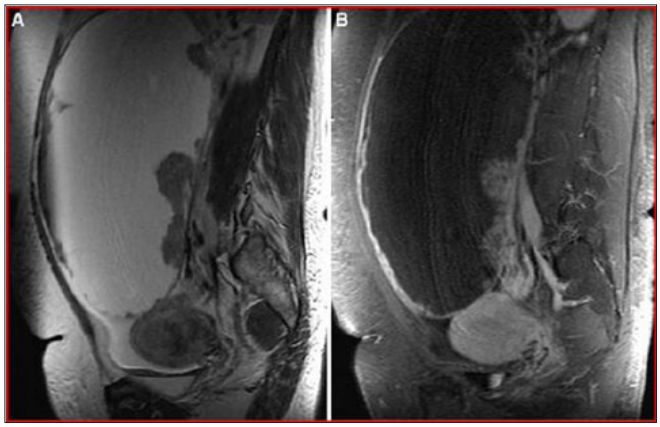

Figure 14 (Koyama et al., 2007)
[Image A, sagittal T2-weighted MRI, demonstrates a large unilocular cystic mass, with multiple low-intensity papillary projections. Image B, T1-weighted MRI with contrast medium, with "fat suppression", highlights the increase in contrast of the papillary shapes within the cystic tumor.]

Metastatic Ovarian Tumor from Breast Cancer

Metastatic disease of the ovary from breast cancer tends to be bilateral in 64% of cases.

Clinically, metastases from breast cancer do not produce symptoms similar to ovarian cancer. Microscopically they appear bilateral and small, with a volume generally smaller than 5 cm.

Typically, as we observe from the images, the masses appear solid and multilocular in appearance and occasionally may contain cysts (Fig.15).

Figure 15 (Koyama et al., 2007)
[Fast spin-echo axial T2 MRI image shows a small, multi-nodular bilateral ovarian tumor (right arrowheads and left arrowheads). The tumor in the left ovary has a strongly intense central area.]

Metastatic Ovarian Cancer from Lymphoma

Radiological findings of secondary involvement of the ovary by lymphoma are extremely rare. The figures reported in MR studies show that ovarian lymphoma appears solid and with diffusely intermediate signal intensity, with septal-like structures that increase in intensity on T2-weighted images.

Furthermore, MR images appear to resemble a Krukenberg tumor, but ovarian tumor secondary to disseminated lymphoma tends to appear more homogeneous than Krukenberg.

The presence of enlarged lymph nodes in locations that are atypical of a lymphatic metastasis of an ovarian cancer, the presence of hepatosplenomegaly or the involvement of other organs, represent additional radiological findings suggestive of the presence of a primary hematological disease (Fig. 16).

It is also interesting to remember that an ovarian metastasis originating from a lymphoma can obviously mimic an ovarian carcinoma. (Donatello et al., 2023).

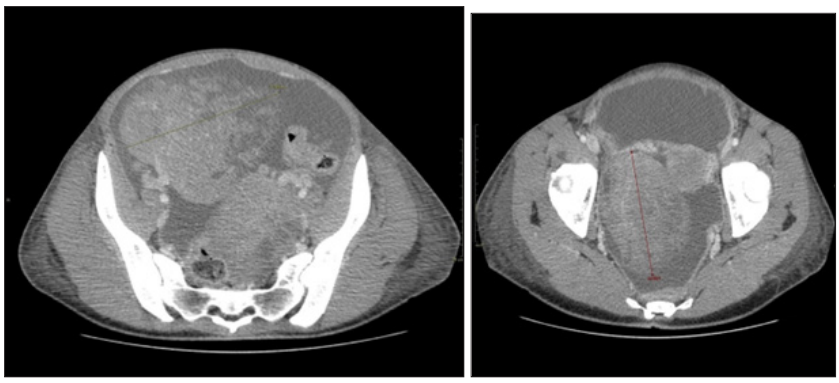

Figure 16 (Donatello et al., 2023)

CT shows the presence in the pelvic area of two voluminous solid formations with regular profiles with preserved cleavage planes, strongly suspicious for lesions of heteroplastic nature with ovarian genesis. It is associated ascites with thickening of the mesentery for peritoneal carcinosis.

Conclusion

We can underline that the radiological images of a secondary ovarian neoplasm differ based on the nature of the primary disease. The author summarizes the radiographic points highlighted in the study as follows:

- The vast majority of gastric cancer metastases are Krukenberg tumors, which are typically bilateral and characterized by the presence of solid masses with heterogeneous signal intensity on T2-weighted MRI images;
- Metastases from colorectal cancer are often bilateral and cystic with a solid component of varying size, and may be accompanied by large areas of necrosis and hemorrhage;
- Metastases from appendiceal tumors appear as ovarian mucinous tumors associated with peritoneal pseudomyxoma;
- Breast cancer metastases, on the other hand, are characterized by small masses;
- Secondary ovarian involvement by disseminated lymphoma is delineated by the presence of bilateral, solid, homogeneous masses. Additional points for diagnosis are the involvement of other organs and the presence of hepatosplenomegaly. A primary ovarian involvement by a lymphoma should be suspected in presence of the "lead vessel" at Power Doppler. (Donatello et al., 2023; Yamada et al., 2003; Crawshaw et al., 2007; Gligorievski et al., 2018; Gregorio et al., 2009; Dalloul et al., 2007; Brown et al., 2001; Liu et al., 2007; Koyama et al., 2007; Testa et al., 2008; Testa et al., 2007)

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