

Preoperative evaluation of ovarian masses: ultrasound and biochemical screening

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Summary

Objective: The preoperative study of an ovarian mass, with a negative dosage of plasmatic BhCG, mainly has the purpose of discriminating between a benign neoplastic mass and a malignant mass. The aim of our work was to evaluate the validity of preoperative screening including a pelvic ultrasound examination and the dosage of some plasmatic tumor markers.

Methods: This is a retrospective study conducted on 78 patients who were referred to the III Division of the Department of Gynaecological Sciences, Perinatology and Puericulture of Rome University "La Sapienza" from January 1st 2001 to December 31st 2001 with a diagnosis of ovarian tumefaction whose origin was still to be determined.

These patients underwent both a transabdominal and transvaginal ultrasound scan and biochemical examination of serum levels of Ca-125, Ca 19-9 and CEA.

Subsequently these patients underwent surgery or medical therapy according to the suspected diagnosis. We then compared our suspected diagnosis with the precise histological diagnosis. Finally, following this comparison, we judged the validity of the proposed screening.

Results: Ultrasound examination is on its own an excellent method for preoperative screening in cases of adnexal tumefactions. However, its association with plasmatic dosages of Ca 125, Ca 19-9 and CEA improves the validity of the screening.

Conclusion: The use of pelvic scanning, both transabdominal and transvaginal, associated with plasmatic dosages of Ca 125, Ca 19-9 and CEA, represents an excellent method of preoperative screening for the evaluation of benign or malignant ovarian tumefactions and for directing the surgeon towards the best therapy.

Key words: Ovarian cancer; Ultrasound; Ca 125; Ca 19-9; CEA.

Introduction

Today ovarian carcinoma is the fifth most frequent gynaecological tumor among the female population. Although it is of relatively low incidence it still has the highest mortality rate among gynaecological tumors [1] which is fundamentally due to the high frequency of late diagnosis, when the neoplasia is already in an advanced stage and becomes difficult to eradicate. This condition may be due to both the scarcity of symptoms in the initial stages of the disease and the absence of efficacious wide scale screening [2]. Thus, we can stress the importance of screening tests which permit an early diagnosis of malignant ovarian neoplasms [3, 4].

Ultrasound and the serological dosage of some tumor markers are considered to have the best research results among the methods studied for diagnosing the presence of an ovarian mass and its nature [5-8], also because they are easily carried out in the analysis of a large number of patients.

The aim of our study was to evaluate the validity of preoperative screening including the plasmatic dosage of some tumor markers [9] and ultrasound examination [10, 11] in diagnosing the presence of an ovarian tumefaction and in giving an indication of eventual malignancy.

In the case of an ovarian mass with benign characteristics we also wished to test the capability of the suggested screening in showing the histological nature of a suspected diagnosis which was then a guide in the choice of the best therapeutic option.

Materials and Methods

Seventy-eight patients were examined at the III Division of the Department of Gynaecological Sciences, Perinatology and Puericulture of Rome University "La Sapienza" between January 1st 2001 and December 31st 2001.

All the patients were diagnosed as having an ovarian tumefaction; only cases with a negative BhCG were considered for our study to avoid the possibility of an ectopic pregnancy. These patients underwent abdominal-pelvic ultrasound and a serological dosage of some tumoral markers.

The pelvic ultrasound was carried out in all cases with a transabdominal probe of 3.5 MHz frequency and with a transvaginal probe of 6.5 MHz frequency.

Every ovarian mass was evaluated for the dimension, thickness and vascularization of its walls, the ultrasound characteristics of its content (solid, liquid, corpuscolated, mixed), the presence of septa in the neoformation and their thickness, and the presence of solid parts inside the cyst.

The bilaterality of the ovarian tumefaction and the eventual association with fluids collected in the Douglas recess or ascites were also evaluated.

The ultrasound examination was then completed performing a Color-doppler scan [12, 13] to investigate the presence of vascularization of the ovarian tumefaction (walls, septa, solid parts) and as an indication of neo-angiogenesis, a typical process in malignant neoplasms.

The tumoral markers dosed in this group of patients were: Ca 125, Ca 19-9, CEA [14, 15].

On the basis of the ultrasound characteristics of the examined ovarian masses and results of the dosage of the tumoral markers we arrived at a point of diagnosis for the malignancy or benignancy of such tumefactions in each patient [16, 17, 18]. If a benign ovarian tumefaction was suspected, we also hypothesized a preoperative diagnosis of its histological nature [19].

The patients then underwent medical treatment (estrogenic therapy) or, as in most cases, surgery (laparoscopy or laparotomy) according to the suspected preoperative diagnosis [20].

Finally we compared the postoperative histological diagnosis with the suspected preoperative one.

The cases which did not undergo surgery were those where the suspected preoperative diagnosis pointed to dysfunctional formations (4 cases); these patients underwent medical therapy with estrogenic therapy for a period of three months and successively a further ultrasound examination was carried out to confirm the suspected diagnosis. In all these patients the above-mentioned cysts disappeared after medical therapy confirming a correct preoperative diagnosis using the proposed screening.

By comparing the preoperative and postoperative data, we evaluated the validity of the screening test.

Results

The average age of the patients was 44,9 (range 17-78). The serological dosage of the tumor markers gave the following results: in 41 cases (53%) the markers were negative; in the remaining 37 cases (47%) the results were positive. Ultrasound investigation indicated a suspected diagnosis of malignancy in 28 patients (36%) and in the remaining 50 patients (64%) benignancy was suspected. This latter group was further divided according to the suspected ultrasound diagnosis on the nature of the analyzed formations: 16 cases of endometriosis, 14 mature struma ovarii, 13 serous cysts, eight cystomas, two thecomas and finally four dysfunctional cysts.

The final histological diagnosis showed the following results: 22 cases (27%) of malignant neoplasias (serous or mucous cystadenocarcinomas of the ovary) and 57 cases (73%) of benign formations. Among the group of patients affected with benign neoplasias the final histological exam showed 14 cases (24%) of endometriosis, 13 cases (23%) of mature struma ovarii, 13 cases (23%) of serous cysts, nine cases (16%) of cystomas (both serous and mucous), four (7%) thecomas and finally four (7%) dysfunctional cysts resolved with medical therapy alone.

Comparing the data obtained after the evaluation of the preoperative biochemical results alone, the ultrasound alone and both used together with those shown by the postoperative histological exam, we analyzed the validity of the proposed screening by calculating the specificity, the sensitivity, the positive predictive values and the negative predictive values.

In differentiating between benign and malignant ovarian tumefactions our screening showed the following values: ultrasound alone showed a sensitivity of 91%, specificity of 88% positive predictive value of 78% and negative predictive value of 95%.

Instead, the dosage of the tumoral markers gave the following values: a sensitivity of 95%, specificity of 71%, positive predictive value of 55% and negative predictive value of 97%.

If we consider the two tests together the values obtained are as follows: sensitivity 92%, specificity 90%, positive predictive value 81% and negative predictive value 96% (Table 1).

If, finally, we consider the ovarian tumefactions thought to be benign after our proposed screening, then with the ultrasound alone a preoperative histological diagnosis proved to be correct in 89,5% of the patients (51 cases); in the remaining 10.5% (6 cases) the postoperative histological exam gave a different result.

Discussion

The results of our study show how the association of the plasmatic dosage of some tumor markers (Ca 125, Ca19-9, CEA) with an ultrasound examination represents an excellent method of screening in patients with ovarian tumefactions, not only for the preoperative individualization of malignant formations, but also for making a diagnosis of the histological type in the case of benign masses.

Ultrasound investigations alone show specificity, sensitivity and positive and negative predictive values which are very close to those obtained using both the diagnostic methods, thus resulting as the first choice of investigation in the study of ovarian tumefactions.

However, we consider it extremely useful to dose the tumoral markers analyzed here to further improve the validity of preoperative screening, above all in those cases in which the ultrasound image alone does not appear sufficient to give a clear diagnostic aspect.

The principal limitations of tumoral markers, and in particular of Ca 125, in discriminating between malignant and benign ovarian tumefactions, is the presence of high values in many cases of endometriosis, above all if there are also implantations in other parts of the pelvis together with ovarian localization.

Table 1. — *Validity of the screening.*

	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Ultrasound	91%	88%	78%	95%
Tumor markers	95%	71%	55%	97%
Tumor markers + Ultrasound	92%	90%	81%	96%

Conclusions

The preoperative study of an ovarian tumefaction, according to our experience, should include an accurate ultrasound examination carried out with both a transabdominal and a transvaginal probe.

Such examinations aim to assess first of all the morphology and dimension of a mass based on the ovary and secondly to evaluate vascularization with the Color-doppler mode and the presence of other signs such as ascites.

Integration with the dosage of tumoral markers, specifically CEA, Ca 125 and Ca 19-9, significantly improves the validity of preoperative screening and is therefore in our opinion to be highly recommended.

Such screening is useful in making as far as possible an early diagnosis of ovarian cancer, thus reducing the high mortality rate still existent in this neoplasia largely due to late diagnoses, and in helping the surgeon to decide on the correct surgical approach (laparoscopy or laparotomy).

Furthermore, the slight invasivity, the high tolerance and the low cost of such exams make this screening easily accessible and available to a large number of patients.

References

- [1] Tortolero-Luna G., Mitchell M. F.: "The epidemiology of ovarian cancer". *J. Cell. Biochem.*, 1995, 23 (suppl.), 200.
- [2] Taylor K. J., Schwartz P. E.: "Screening for early ovarian cancer". *Radiology*, 1994, 192 (1), 1.
- [3] Taylor K. J., Schwartz P. E.: "Cancer screening in a high risk population: a clinical trial". *Ultrasound. Med. Biol.*, 2001, 27 (4), 461.
- [4] Quinn M. A.: "Screening for ovarian cancer". *Aust. Fam. Physician*, 2001, 30 (6), 530.
- [5] Westhoff C.: "Current status of ultrasound for ovarian cancer". *Gynaecol. Oncol.*, 1995, 55 (3), 34.
- [6] Karlan B. Y., Platt L. D.: "The current status of US and Color Doppler imaging in the screening for ovarian cancer". *Gynaecol. Oncol.*, 1995, 55 (2), 28.
- [7] Von Schippl M., Rusting G. J.: "Circulating tumor markers in ovarian tumors". *Forum (Genova)*, 2000, 10 (4), 383.
- [8] Kehoe S., Selman T.: "Tumor markers in ovarian cancer". *Hosp. Med.*, 2001, 62 (8), 452.
- [9] Maggino T., Gadducci A.: "Serum markers as prognostic factors in epithelial ovarian cancer: a overview". *Eur. J. Gynecol. Oncol.*, 2000, 21 (1), 64.
- [10] Grab D., Flock F., Stohr I., Nussle K., Rieber A., Fenchel S. *et al.*: "Classification of asymptomatic adnexal masses by ultrasound, magnetic resonance imaging, and positron emission tomography". *Gynecol. Oncol.*, 2000, 77 (3), 454.
- [11] Menon U., Talaat A., Rosenthal A. N., Macdonald N. D., Jeyarajah A. R., Skates S. J. *et al.*: "Performance of ultrasound as a second line test to serum CA125 in ovarian cancer screening". *Br. J. Obstet. Gynaecol.*, 2000, 107 (2), 165.
- [12] Antonic J., Rakar S.: "Validity of Color and Power Doppler US and tumor marker Ca 125 in differentiation between benign and malignant ovarian cancer". *Eur. J. Gynaecol.*, 1995, 17 (1), 29.
- [13] Shy K., Dubinsky T.: "Is Color Doppler ultrasound useful in diagnosing ovarian cancer?". *Clin. Obstet. Gynecol.*, 1999, 42 (4), 902.
- [14] Toki T., Kubota J., Lu X., Nakayama K.: "Immunohistochemical analysis of CA125, CA19-9, and Ki-67 in stage III or IV endometriosis: positive correlation between serum CA125 level and endometriotic epithelial cell proliferation". *Acta Obstet. Gynecol. Scand.*, 2000, 79 (9), 771.
- [15] Morgante G., La Marca A., Ditto A., De Leo V.: "Comparison of two malignancy risk indices based on serum CA125, ultrasound score and menopausal status in the diagnosis of ovarian masses". *Br. J. Obstet. Gynaecol.*, 1999, 106 (6), 524.
- [16] Morgan A.: "Adnexal Mass evaluation in the emergency department". *Emer. Med. Clin. North Am.*, 2001, 19 (3), 799.
- [17] Takayashi K., Kurioka H., Irikoma M., Ozaki T., Kanasaki H., Miyazaki K.: "Benign or malignant ovarian neoplasm and ovarian endometriomas". *J. Am. Assoc. Gynecol. Laparosc.*, 2001, 8 (2), 278.
- [18] Gotlieb W. H., Soriano D., Achiron R., Zalel Y., Davidson B., Kopolovi J. *et al.*: "CA125 measurement and ultrasonography in borderline tumors of the ovary". *Am. J. Obstet. Gynecol.*, 2000, 183 (3), 541.
- [19] Chechia A., Koubaa A., Makhlof T., el-Hitmi N., Messaoudi Y., Terras K. *et al.*: "Les tumeurs fibrothecales de l'ovaire. A propos de 12 observations". *Gynecol. Obstet. Fertil.*, 2001, 29 (5), 349.
- [20] Canis M., Botchorishvili R., Manhes H., Wattiez A., Mage G., Pouly J. L. *et al.*: "Semin. Surg. Oncol.". 2000, 19 (1), 28.

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