

Fine needle aspiration cytology of the ovary: Is it reliable?

**K. Papathanasiou, Assoc. Prof.; C. Giannoulis, Assoc. Prof.; D. Dovas, M.D.; A. Tolikas, M.D.;
T. Tantanasis, Lecturer; J.M. Tzafettas, Prof.**

Department of Obstetrics and Gynaecology, Hippokration Hospital, Thessaloniki (Greece)

Summary

Purpose of investigation: The purpose of this study was to evaluate the cytologic findings from the fluid of ovarian cysts in comparison with the histologic diagnosis.

Methods: Over a four-year period all women with single ovarian cysts and no evidence of malignancy from ultrasound examination and tumour marker levels were included in the study. Prior to removal of the cyst, fluid was aspirated from the cyst and prepared for cytologic examination. Subsequently the ovarian cyst wall and biopsy from the ovary were sent for histologic examination. The cytologic findings were compared to the histologic diagnosis.

Results: The material of the study was 120 ovarian specimens from 107 women. Twenty-four (20%) of the specimens submitted for cytology were non diagnostic and a comparison between cytologic and histologic findings was possible in 96 cases. The sensitivity and the specificity of fine needle aspiration (FNA) cytology of the ovary was 25% and 97%, respectively.

Conclusions: FNA cytology of the ovary is an accurate method for predicting benign ovarian histologic findings in carefully selected populations.

Key words: Ovarian cyst; FNA; Cytologic findings; Histologic diagnosis of ovarian cysts.

Introduction

Fine needle aspiration (FNA) of ovarian cysts has been proposed as an alternative to surgery (either laparoscopy or laparotomy) [1]. The clinical experience has shown that the procedure has minimal complications and is well tolerated by patients [2]. Despite many controversial views regarding its safety, mainly because of the risk of rupture of cystic ovarian tumors with resultant tumour dissemination, aspiration cytology has been accepted as an innocuous procedure [3, 4]. This seems to be the case when certain criteria are met prior to the procedure. These include sonographically benign appearance of the cyst (unilateral, unilocular, homogenous, anechogenic with a diameter less than 7 cm) and serum levels of CA125 and CA19/9 less than 35U/ml [5]. Another significant issue is the diagnostic accuracy of the ovarian cyst fluid cytologic assessment. There is some evidence from previously reported studies that the cytologic findings from ovarian cysts do not correlate with the ovarian histologic findings [6-8]. The aim of this study was to compare the cytologic findings of the fluid of ovarian cysts with the histologic diagnosis of the ovaries which were subsequently removed surgically.

Material and Methods

During a four-year period ovarian cyst fluid aspirate was obtained from 120 ovaries. Only women with intact single ovarian cysts were included in the study and the cyst fluid was

obtained during the surgical procedure (either laparoscopy or laparotomy), using a Cameco cytologic aspirator (Cameco, Sweden) with a 10 ml syringe and a 21-gauge needle. The tip of the needle was directed into the cyst and not into the stroma of the ovary. The aspirate was mixed with a solution of 50% of ethanol and carbowax. The material was then immediately sent to the cytology department of the hospital and a slide preparation was made for examination. All specimens were prepared using the Papanicolaou-stained cytospin technique. A single cytologist examined all specimens and was blinded to the appearance of the ovary.

The cytologic findings were classified into non-diagnostic, benign and malignant neoplasms.

Following aspiration of the ovarian cyst, the ovarian specimens consisting of the capsule of the cyst and a biopsy from the surface of the ovary with a diameter around 1 cm, were submitted for histological examination to the pathology department of Hippokration Hospital. Preparation of the ovarian specimens was performed by staining with haematoxylin-eosin. A single pathologist examined all specimens and was blinded to the cytologic findings. The histologic findings were classified according to the WHO guideline for histologic classification of the ovary.

Results

The study material consisted of 120 ovarian specimens from 107 women. Twenty-two out of the 107 women (20.5%) were postmenopausal. The average age of women was 46 years (range 25-55). Eighty-nine ovarian cysts were removed laparoscopically and 31 by laparotomy. All ovaries had single cysts and were intact. The size of the ovarian cysts ranged from 2 to 6 cm (mean size 4 cm). The malignancy potential of the cysts was

investigated and three days prior to surgery the women had pelvic ultrasound and serum tumour marker (CA125 and CA19/9) levels performed. The ultrasound findings were suggestive of benign disease (unilocular, homogeneous and anechogenic). The levels of CA125 and CA19/9 were less than 35U/ml.

The histologic results revealed 117 benign ovarian cysts and three borderline carcinomas with low malignancy potential. The histologic diagnosis as far as benign cysts are concerned was 39 functional (29 follicular cysts and 10 corpus luteum cysts), 51 epithelial (31 serous cystadenomas, 11 mucinous cystadenomas and 9 endometriomata) and 27 germ cell (all of them dermoid cysts). The three borderline ovarian carcinomas were all epithelial (2 serous and one mucinous cystadenoma). A detailed analysis of the histologic findings is shown in Table 1.

Table 1. — *Ovarian histologic findings (n = 120).*

Histologic Diagnosis	Benign	Malignant
<i>Functional</i>	39	0
Follicular	29	0
Corpus luteum	10	0
<i>Epithelial</i>	51	3
Serous cystadenoma	31	2
Mucinous cystadenoma	11	1
Endometrioma	9	0
<i>Germ cell</i>	27	0
Dermoid	27	0

In 24 (20%) of the cytologic specimens no diagnosis could be made, mainly due to the acellularity of the specimens. The histologic examination of these specimens revealed 23 benign ovarian tumours and one borderline serous cystadenoma. A comparison of the cytologic findings with the histologic diagnosis in the rest of the 96 specimens is shown in Table 2. Sensitivity of the cytologic evaluation of the ovarian cysts following FNA was 50% and specificity of the method was 97% with a false positive rate of 75% and a false negative rate of 1%.

Table 2. — *Comparison of cytologic findings with histologic diagnosis (n = 96).*

Cytologic findings	Histologic findings	
	Benign	Malignant
Benign	91	1
Malignant	3	1

Discussion

The widespread use of ultrasound has made the diagnosis of ovarian cysts quite common. The challenge for the clinician is to determine which ovarian cysts have a high malignancy potential and need management from specialists possibly in a tertiary center and which are more likely to be functional, particularly in premenopausal women, with an increased likelihood to resolve spontaneously. Many tests have been proposed

for the initial evaluation of ovarian cysts but unfortunately none of them can accurately predict the histologic diagnosis. Possibly the combination of many of these tests including serum tumour markers, sonographic findings, computed tomography (CT) and magnetic resonance imaging (MRI) scanning as well as Doppler studies can give more information regarding the possible histologic diagnosis, but all these investigations have their limitations.

One attractive approach seems to be the cytologic evaluation of the ovarian cyst contents following aspiration of the ovarian cyst fluid using a fine needle under sonographic guidance. This can be performed relatively easily with minor complications [1, 3, 9]. Although substantial concerns have been raised regarding the safety of this technique in the presence of malignancy, mainly because of the risk of dissemination of cancer cells during the procedure, there are reports which support its use if certain criteria are met such as a sonographically benign appearance of the cyst (unilateral, unilocular, homogeneous, anechogenic with a diameter less than 7 cm) and serum levels of CA125 and CA19/9 less than 35 U/ml [5, 10].

There is also evidence from previous studies that following FNA of ovarian cysts there is a relatively large proportion of non-diagnostic specimens, mainly due to the small number of cells contained in the cyst fluid, ranging from 11% to 56% [8, 14]. One possible explanation for this could be the fact that in many cases the tip of the needle is directed into the cavity of the cyst and not into the stroma of the ovary resulting in a significant number of acellular specimens. Our study was designed to mimic exactly the FNA procedure under sonographic guidance by directing the needle into the cavity of the ovarian cyst. Following this technique we had 24 cases of non-diagnostic cytologic specimens (20%).

We had one case of borderline ovarian carcinoma with a non diagnostic cytologic specimen, devoid of both malignant and non-malignant cells. Cases of ovarian cancer with the primary lesion far from the cyst have been described which resulted in very few or no malignant cells in the cyst fluid [6]. The consequence of this is an acellular specimen inadequate to establish the diagnosis and misleading the clinician.

The cytologic evaluation of various nodules such as those from the breast, lung and thyroid following FNA is proven to be reliable [12]. There is however conflicting evidence regarding the diagnostic accuracy of the ovarian cyst cytologic evaluation. According to the current literature the sensitivity of the method ranges from 25% to 75% [6, 8] in various studies. Our study revealed that fine needle aspiration cytology of the ovary has 50% sensitivity and 97% specificity for the diagnosis of ovarian cysts. This shows that the method is not accurate enough to predict a malignancy in histology but has a great power to specify in which cases the histology is more likely to show a benign ovarian cyst, with a false negative rate of only 1%.

The power of our study lies on the fact that all the women had ultrasound examination and tumour marker

levels non suggestive of a possible malignancy prior to the aspiration. By that, we tried to mimic closely the most common scenario "indicating" FNA cytology of the ovary. Our study suggests that a careful selection of patients with ultrasound findings not indicating malignancy and normal tumour marker levels (CA125, CA19/9) can significantly increase the specificity of the method rendering FNA cytology of the ovary a significant diagnostic tool.

Another significant issue is that two out of three borderline carcinomas found in our population of women were in the postmenopausal group. This means that FNA cytology is possibly more powerful in excluding malignancy, if the menopausal status of the woman is taken into account.

There is some evidence from previous studies that the method is complicated with a high risk of recurrence of the ovarian cysts so there are concerns about its place as a treatment option [1, 13]. Even if this is the case, it seems that FNA cytology still has a role as a treatment option in specific groups of patients such as in young women with functional cysts, pregnant women or women unsuitable for surgery.

Conclusion

In carefully selected premenopausal women, with normal serum tumour markers and sonographic findings non suggestive of malignant disease (unilocular, homogeneous and anechogenic ovarian cysts with the largest diameter less than 6 cm), a cytologic report negative for malignancy indicates that the histologic diagnosis is extremely unlikely to reveal malignant disease. This means that FNA cytology of the ovary maybe used as a second-line diagnostic tool for ovarian cysts and possibly as a treatment option.

Non-diagnostic cytologic specimens, devoid of cells, need to be interpreted cautiously. The main reason for this is the fact that in some cases of cancer the distribution of the cancer cells is such that none of them can be found inside the cyst content.

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Address reprint requests to:
K. PAPATHANASIOU, Assoc. Prof.
2nd Univ. Dept. Ob./Gyn.
Hippokraton Hosp.
49 Konstantinoupoleos Street
546 42 Thessaloniki (Greece)