

Fine Needle Aspiration of Unilocular Ovarian Cysts - a Cytohistological Correlation

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Abstract

Objective: To assess the diagnostic efficacy of Fine Needle Aspiration Cytology in differentiating neoplastic and non-neoplastic dysfunctional ovarian cysts - cytological findings to be verified with histology of excised cyst.

Methods: In this prospective study fifty-three cases with unilocular nonseptate ovarian cystic masses, detected on ultrasound examination were subjected to ultrasound guided fine needle aspiration of the cyst contents at Department of Pathology, Allama Iqbal Medical College Lahore, from January 1999 - January 2000. Aspirated fluid was examined cytologically using Giemsa stain on the smears prepared from centrifuged deposit. The same cyst removed surgically was examined histologically and cytohistological correlation was carried out.

Results: In this series of 53 cases, histologically confirmed break up of various types of cysts was follicular cysts (n=25), leuteal cysts (n=6), serous cysts (n=15), mucous cysts (N=4) and Endometriotic cysts (n=3). Non-diagnostic fine needle aspirate was obtained in 19/53 cases, majority being the follicular cysts. The cytohistological correlation revealed no false positive but 40% false negative results for follicular cysts on cytological examination of the aspirate. Hence the specificity and sensitivity for cytological diagnosis of follicular cyst was 100% and 60% respectively. For leuteal cysts, false positive and false negative results on cytological examination were 0% and 16.6% respectively with a specificity and sensitivity value of 100% and 83% respectively. For neoplastic serous cysts cytologically false positive and false negative diagnosis was 0% and 46.6% respectively with specificity and sensitivity of 100% and 53%. For mucinous cystadenomas sensitivity and specificity of cytological diagnosis was 100%. For endometriotic cysts a sensitivity of 67% and specificity of 100% was procured with cytological evaluation.

Conclusion: Guided fine needle aspiration cytology may prove to be one of the most valuable and acceptable tools in the differential diagnosis of ovarian cystic lesions. (JPMA 54:266;2004).

Introduction

Cystic lesions in the ovary are fairly common being encountered mostly in reproductive age group. The clinical presentation is variable, majority being discovered accidentally during pelvic ultrasound examination. A prevalence rate of 6.6% has been reported for cystic ovarian masses on random screening through trans-vaginal ultrasound.¹ These cysts are broadly categorized into dysfunctional and neoplastic types.² The latter in turn being either benign or malignant. Ultrasonography is used as one of the recommended techniques for discriminating benign and malignant ovarian cysts.³ Benign nature is favoured by the presence of unilocular nonseptate thin walled cyst with no solid areas.⁴

Whereas features suggesting malignancy include multiloculation, thick septas and presence of solid foci in the wall.⁵ Various types of benign neoplastic cysts present considerable overlapping features with the functional ovarian cysts on ultrasound examination. The clinical significance of these two types of cysts however, is very different for the gynaecologist. The functional cysts are of less serious concern where expectant follow up resulted in 82% disappearing in a couple of weeks to months.¹ For various types of neoplastic cysts however, surgical excision remains the treatment of choice.⁶ The combination of sonography and needle aspiration cytology serves as a particularly valuable technique in differentiating these cyst types.⁶ Hence the diagnostic routine of clinical examination, ultrasound and laparoscopic examination has now been expanded to include cytological screening of the fluid aspirated from ovarian cysts.⁷ Considering the economic and social constraints of our general population it is highly desirable that any superfluous surgery be avoided. The present prospective study was, therefore, undertaken to evaluate the diagnostic efficacy of cytological examination of ovarian cyst fluid for differentiating between benign neoplastic and the functional ovarian cysts.

Patients and Methods

Fifty three cases were prospectively selected from Gynaecology wards of Jinnah Hospital and Lady Willingdon Hospital, Lahore. Inclusion criteria were presence of cystic lesion in the ovary on ultrasound examination showing unilocular, non-septate, thin walled cyst with no solid areas in the wall. Exclusion criteria were suggestion of malignancy on ultrasound examination and symptom of acute pain. Fine Needle Aspiration was carried out under ultrasound guidance using a Real Time Sector scanner (Siemens Sonoline SL-2). Spinal aspiration needle of 20 gauge was used attached to a 50 ml disposable syringe. The aspirate was centrifuged at a speed of 1000 revolutions/min. for 10 minutes. The sedimented cell button was used for

making smears which were air dried and stained with Giemsa stain. The cytological examination was later correlated with the histology of the same cyst removed during laparotomy. From the removed cyst wall 1 block/cm were taken, processed with the recommended procedure for paraffin blocks preparation, 2-4/m thick sections were cut, stained with Haematoxylin and Eosin stain and examined for histological features. The cytological diagnosis was thus verified and false negatives and false positive results for the various cyst types were recorded.

Results

Fifty-three patients ranging in age between 24 and 68 years were included in this study. All had unilocular, non-septate, thin walled ovarian cyst, on ultrasound examination. Nondiagnostic/acellular aspirate was obtained in 19/53 cases, maximum being in cases of follicular cysts (10/15).

Table 1. Cytohistological correlation.

Type of cyst	Histological diagnosis	Cytological diagnosis	False positive (%)	False negative (%)
Follicular	25	15	-	40.0
Leuteal	6	5	-	16.6
Serous	15	8	-	46.6
Mucous	4	4	-	-
Endometriotic	3	2	-	33.3

Table 2. Sensitivity and specificity of fine needle aspiration for various cysts.

Type of cyst	Cytological diagnosis	Sensitivity (%)	Specificity (%)
Follicular	15	60.0	100.0
Luteal	5	83.0	100.0
Serous	8	53.0	100.0
Mucous	4	100.0	100.0
Endometriotic	2	67.0	100.0

In diagnostically adequate cellular aspirates from different cyst types, the cytological characteristics of exfoliated cells presented classical diagnostic morphology. Follicular cysts revealed loosely coherent sheets of polyhedral cells with majority of cell clusters showing uneven irregular boundary. Leuteal cysts revealed small groups of

groups of polyhedral cells, being larger with abundant cytoplasm showing microvesicles or granularity. Nuclei were eccentric with 1-2 nucleoli. In neoplastic benign serous cyst adenomas the desquamated cells formed compact groups or monolayered sheets or rare papillary formations. These were small cells with small nuclei and inconspicuous nucleoli. In cases of mucinous cyst adenomas, cells formed loose clusters and groups with no overlapping or tight crowding. Cell outlines were clear and cytoplasm was dense and abundant. In some clusters honeycombing was seen. In endometriotic cysts, sheets of endometrial cells were seen as monolayered layout of epithelial cells. These were small cells with scanty cytoplasm. Background revealed plenty of degenerated RBCs, pigmented and non-pigmented macrophages.

In this study histological examination of the surgically removed cysts was used for verifying the cytological diagnosis. Cytohistological correlation thus carried out is depicted in table-1 showing the false positive and false negative results and alongwith sensitivity and specificity for each category of cysts in Table 2. Non-diagnostic acellular aspirate was the main confounding factor in cytological diagnosis. Those cases where representative cell population was present in the aspirate could all be diagnosed correctly on cytology, yielding a specificity of 100% for cytological diagnosis in all categories of cystic masses.

Discussion

Basic categorization of ovarian cysts into dysfunctional and neoplastic cysts is extremely important from clinical point of view. To by pass the surgical excision of the cyst for this differentiation, cytological evaluation of the fine needle aspirates of the cyst contents has been widely accepted.⁸

In our study cytological evaluation of the aspirated fluid revealed non-diagnostic features in several cases. This was due to either aspiration of acellular fluid or due to the presence of diagnostically insignificant macrophages, R.B.Cs and inflammatory cells. Several studies have highlighted this pitfall of cytological diagnosis.^{9,10} Maximum incidence has been reported in cases of follicular cysts, in the range of 50-52%.^{9,11} Our findings also support these observations with 40% of our histologically proven follicular cysts showing non-diagnostic aspirates. This acts as the main confounding factor in reducing the sensitivity of cytological diagnosis, reported previously as well.¹² For leuteal cysts the non diagnostic aspirate was obtained in only 20% of our cases. This however, may not be the true reflection because of the small number of cases of this cyst type in the present series. In the category of neoplastic cysts 46.6% of the serous cysts yielded non-

diagnostic aspirates in our study. Previous studies have reported even higher frequency (55%).⁹ In cases of mucous cysts, some authors have reported figures as high as 43% for procurement of cytologically non diagnostic aspirates.⁹ All our cases of mucous cyst adenomas however yielded diagnostically appropriate aspirates. Here once again small number of cases for this type of cyst has to be taken into account in our series. Non-diagnostic aspirates in cases of endometriotic cysts in our study was encountered in 33.3% cases. An almost double figure is reported, however, for this type of cyst by previous workers.⁹

Analysing the cytological examination, 15 of the cystic lesions were labeled as follicular cysts. In accordance with the previous reports the desquamated cells resembled granulosa cells in all cases. A diagnostic pitfall however, in the highly cellular aspirates from follicular cysts is the overlapping cytological appearance between granulosa lining cells of follicular cysts and epithelial cells of serous cyst adenoma.¹³ In such debatable situations use of ancillary technique is highly recommended such as anti-inhibin immunocytochemical staining where granulosa cells are strongly positive and serous cells are not.¹³ The most helpful technique remains however, the estradiol (E2) assay of the cyst fluid with a cut off limit of >20nmol/L (>800 pg/ml).^{9,14,15} In the study evaluating estradiol and progesterone levels in follicular cysts alongwith cytology, a 100% sensitivity and 94.7% specificity for diagnosis of functional cysts has been reported.¹⁵ Thus multidisciplinary approach for the differentiation of neoplastic and dysfunctional cysts is strongly recommended including the tumour markers as CEA & CA-125.¹⁶ Combination of low CA-125 level and estradiol level >1000 Pg/ml has been proposed as supportive of diagnosis of a "dysfunctional cyst".¹⁷ Cytological features of leuteal cysts in our study tallied with the cell morphology reported in previous studies.^{18,9} However, unlike reports of previous several workers¹⁸⁻²⁰ we did not encounter any atypical cellular changes in our cases of leuteal cysts, attributed to excessive hormonal stimulation.

In our series of 15 cases of histologically proven serous cyst adenomas, 46.6% false negative result were encountered on cytology. This diagnostic challenge has been highlighted in several studies^{15,16} attributed to atrophic epithelial lining. This consistently reported observation highlights the significance of adjunctive techniques and multidisciplinary approach for accurate diagnosis. Another pitfall in highly cellular aspirates from serous cysts is the morphological overlapping with proliferative/borderline tumours.⁹ We did not face this problem in our series where all 8 adequate aspirates revealed diagnostic cytological morphology. For cases of mucous cyst adenomas we procured diagnostic aspirates in

all the histologically proven cysts of this type. The cellular features were distinctive and posed little morphological overlapping with other cystic lesions. This concurs with the 96.7% correct cytological diagnosis reported for this type of cyst.¹⁴ Some studies, however, report various pitfalls in cytological diagnosis of mucous cysts in the form of presence of bizarre nuclei suggestive of malignancy or acellular aspirates.^{9,15,16} Endometriotic cysts are a great diagnostic challenge even on histological examination.²¹ Accordingly the cytological diagnosis carries the same reputation where some studies report 63.6% false negative cytological diagnosis for this type of cyst.⁹ Considering the histologically high incidence of denuded lining of the cyst and its replacement by pigmented macrophages and fibrin, frequent procurement of cytologically non-diagnostic aspirates is an acceptable observation. In diagnostic aspirates, presence of endometrial cell groups amongst pigmented and non-pigmented macrophages and abundant RBCs was our finding, tallying with the similar observations of previous workers.

In the present study Gold standard for verification of our cytological diagnosis was histological examination of the removed cyst followed by cytohistological correlation. None of the previous such studies has reported a 100% sensitivity or specificity of cytological diagnosis with reported frequency ranging between 25-90%. Higgins et al reported a sensitivity of only 25% and specificity of 90% suggesting that cytological examination does not accurately predict the histological findings.²² Koss et al supporting this observation emphasized that 100% accuracy is an unrealistic expectation in cytological diagnosis.²³ In the present study we analysed each type of ovarian cyst encountered for cytohistological correlation. As depicted in Table 2, the sensitivity of all types of cysts ranged between 60-100%. The main confounding factor was procurement of acellular fluid or fluid with diagnostically irrelevant cells. Specificity however was 100% in our study. This reflects that in aspirates with adequate cell population the desquamated cells were diagnostically reflecting the cyst lining when compared with histology.

Conclusion

The cytological interpretation of aspirates from ovarian cysts represents one of the most challenging fields in diagnostic cytology. Pathologist's ability to distinguish various cysts type with Fine Needle Aspirate needs experience and ample exposure to aspirates. Thus with gynaecol-

ogists resorting more to this procedure and pathologists gaining confidence in their ability to evaluate samples correctly, aspiration cytology may prove to be one of the most valuable tools in the diagnosis of cystic lesions.

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