Original Article

Utility of Image Guided Fine Needle Aspiration in the Diagnosis of Ovarian Masses: A Cytohistopathological Correlation

Menka Khanna*, Manisha Sharma, Mridu Manjari, Manas Madan, Kiranjot Kaur and Shruti Gupta

Department of Pathology, SGRDIMSAR, Amritsar, India

Keywords: *Image Guided FNAC, Ovary, Neoplasms, Histopathological Correlation*

ABSTRACT

Background: The incidence of ovarian masses has increased over the past two decades and is one of the leading causes of cancer-related deaths globally. Although histopathology remains the gold standard, in recent times, image-guided aspiration is being increasingly used as a rapid, inexpensive and efficient method for the pre-operative diagnosis of ovarian masses. The present study was performed to evaluate the efficacy of image guided FNAC in diagnosis of ovarian masses in comparison with histopathology and to assess the limitations of cytological interpretation.

Methods: The study was conducted on 92 cases of ovarian masses which were evaluated by image guided FNAC. Sensitivity, specificity and diagnostic accuracy were calculated using histopathology as gold standard.

Results: Cytological diagnosis was obtained in all the 92 patients with ovarian masses followed by histopathological examination. The cytological diagnosis was grouped into 2 categories- Benign/Possibly Benign (60 cases) and Malignant/Suspicious of malignancy (32 cases). On cytohistological correlation it was found that a correct diagnosis was made in 86 cases, resulting in a diagnostic accuracy of 93.4%, sensitivity of 84.3 % and specificity of 98.3%.

Conclusion: Image guided FNAC seems to be a relatively safe, simple, fast and cost-effective procedure where most ovarian malignancies can be correctly diagnosed with a high accuracy.

***Corresponding author:**
Dr. Menka Khanna, Department of Pathology, SGRDIMSAR, Amritsar, India
Phone: +91 9464986355
Email: mona74_khanna@yahoo.co.in

Introduction

Ovarian neoplasms are a heterogenous group comprising of benign and malignant tumors of epithelial, stromal and germ cell origin. [1] The incidence of malignant ovarian masses has increased over the past two decades and is one of the leading causes of cancer-related deaths globally. The majority of ovarian masses are benign but almost two-thirds of malignant ovarian tumours present at an advanced stage. [2] Fine-needle aspiration cytology (FNAC) of these ovarian masses is offer the potential to decrease the need for surgical procedures in these women. The use of radiological techniques can ensure greater accuracy and reduction in false negativity in the assessment of tumors by increasing the yield of cytological specimens. Differing from blind procedure, ultrasound or CT guided FNAC can localize the most suspicious areas in tumor mass and therefore help in taking the sample from the most representative site. [3,4,5] Geier and Strecker have suggested that FNAC should be used for (1) recurrent and metastatic tumors, (2) suspected benign ovarian cysts and (3) when the patient›s condition is unsuitable for laprotomy. [6] However, till today, gynaecologists all over the world are hesitant to accept the role of FNAC on pelvic masses because of the controversial opinion about the potential risk of intraperitoneal tumor implantation, particularly of ovarian tumors, although the risk of carcinoma cell seeding within the abdominal cavity due to contamination by needles is overestimated and has not been documented. [7] Although histopathology remains the gold standard, in recent times, image-guided aspiration is being increasingly used as a rapid, inexpensive and efficient method for the pre-operative diagnosis of ovarian masses.[8]The present study was performed to evaluate the role of image guided FNAC in pre-operative cytological diagnosis of ovarian masses in comparison with histopathology and to assess the discrepancies and limitations of cytological diagnoses.

Materials and Methods

The study was conducted on 92 patients who presented with the ovarian masses diagnosed clinically or radiologically. Following the clinical examination, informed consent was taken from the patients. USG/CT guided FNAC was done using 22-23 gauge needle attached to a 20 ml syringe. Smears were prepared from the aspirate, fixed in 95% alcohol and stained with May Grumwald Giemsa and Hematoxylin and eosin stains. In the cases where cyst fluid was aspirated, it was subjected to cytocentrifugation and the sediment was stained by the similar methods. No major complications were observed in any of the patients. The cytological diagnosis was compared with histological diagnosis. Taking histological diagnosis as the gold standard, various statistical calculations were done.

Result

A total of 92 cases of ovarian mass lesions were evaluated on cytological smears. The most common presenting feature was lower abdominal pain (80.5%), followed by abdominal distension (50%), menstrual irregularity (27.7%) and weight loss (8.3%).

The age of the patients range from 18 to 65 years, with maximum patients in 4th decade of life. USG / CT helped in the assessment of type of mass lesion (cystic/solid) along with its size, location and extent and thus augmented the cytological diagnosis. The cytological diagnoses were made as benign/possibly benign and malignant/suspicious of malignancy.

Considering the histopathological diagnosis as gold standard, the cyto-histopathological correlation was done in these cases.

On histopathology 60 cases were diagnosed as non malignant, out of which 8 cases were of non-neoplastic cysts and 52 cases were of benign ovarian tumors. Serous cystadenomas were the most common (27) benign ovarian tumor followed by mucinous cystadenoma (14) , mature teratoma (8) and fibroma (2).There was one case each of thecoma and sclerosing stromal tumor.(Table 1). A histopathological diagnosis of malignancy was given in 32 cases. Serous cystadenocarcinoma was the most common (16) histopathology diagnosis among malignant lesions followed by mucinous cystadenocarcinomas (5) and serous borderline tumor (3). There were 2 cases each of mucinous borderline tumor, dysgerminoma and granulosa cell tomor and one case each of immature teratoma and mixed germ cell tumor. (Table 2) Mature teratomas on histopathology show cyst lined by keratinising stratified squamous epithelium along with differentiated glandular epithelium,neuroglia and other elements.(Figure 1) However in immature teratoma islands of neuroepithelium were clearly identified.

The sections in cystadenomas showed cysts lined by single layer of columnar epithelium which was ciliated in serous tumors, where as in borderline cases complex papillary structures lined by epithelium with stratification and nuclear atypia were seen; clear cut stromal invasion was identified in cystadenocarcinomas. (Figure 2) Sclerosing stromal tumor showed lobular arrangement with alternate hyper and hypocellular areas comprised of oval to spindle shaped cells with many dilated blood vessels in hypocellular areas. The sections in granulosa cell tumor showed sheets of oval to spindle cells with nuclear grooves and forming Call Exner bodies. (Figure3) FNAC from serous cystadenoma mostly yielded straw coloured fluid and the smears prepared

from the centrifuged deposits showed papillary fragments with bland nuclei and cyst macrophages. Aspirates from benign cystic teratoma showed mature squamous cells in a dirty background (Figure1). Mucinous cystadenomas showed isolated clusters of columnar epithelial cells with basally placed nuclei against mucinous background. Serous cystadenocarcinoma showed papillary fragments comprising of hyperchromatic pleomorphic cells having high N/C ratio (Figure2). The mucin producing cells with malignant nuclear features against mucinous background were diagnosed as mucinous cystadenocarcinoma. Cytology of granulosa cell tumor comprised of uniform round nuclei with microfillicle formation and nuclear grooving (Figure3).

Of the 60 cases which were histopathologically diagnosed as non-neoplastic cysts (8) or benign neoplasms (52), 59 cases were diagnosed as benign or possibly benign on cytology and one case of sclerosing stromal tumor was falsely reported to be suspicious of malignancy. Of the 32 cases diagnosed as malignant tumors a cytological diagnosis of malignancy was made in 27 cases and 5 cases(including 3 cases of borderline tumors, one case each of mucinous cystadenocarcinoma and immature teratoma) were reported to be falsely negative for malignancy. In borderline tumors the smears showed few papillae lined by cells lacking much of atypia, conspicuous nucleoli or mitotic figures.(Figure.4) One case of mucinous cystadenocarcinoma on cytology showed mainly mucin and scattered epithelial cells and the solid area of the tumor was not sampled adequately. The cytological smears in immature teratoma just showed few squamous and round to oval cells along with eosinophilic agranular material. The smears in case of sclerosing stromal tumor showed atypical oval to spindle cells along Call-Exner bodies like structures.

For all the 92 cases, the sensitivity and specificity of cytological diagnosis considering the histopathological diagnosis as gold standard were 84.3 % and 98.3% respectively with overall diagnostic accuracy of 93.4 %. The positive predictive value and negative predictive value were 96.4% and 92.1% respectively.

Table 1: Comparative analysis of confirmed benign ovarian lesions (on histopathology) with their corresponding cytological diagnosis.

Histopathological Diagnosis		Cytological Diagnosis	
		Benign/Possibly benign	False positive for malignancy
Non Neoplastic Cysts	Follicular cyst (n=4)	4	
	Endometriotic cyst (n=2)	2	
	Corpus luteal cyst (n=2)	1	
Benign Neoplasms	Fibroma (n=2)	2	
	Thecoma (n=1)	1	
	Sclerosing stromal tumor (n=1)	0	1
	Serous cystadenoma (n=27)	27	
	Mucinous cystadenoma (n=14)	14	
	Benign cystic teratoma (n=8)	8	

Table 2: Comparative analysis of confirmed Malignant ovarian lesions (on histopathology) and their corresponding cytological diagnosis.

Histopathological diagnosis	Cytological diagnosis	
	Malignant / suspicious of malignancy	False negative for malignancy
Serous cystadenocarcinoma (n=16)	16	
Mucinous cystadenocarcinoma (n=5)	4	1
Serous borderline tumors (n=3)	1	2
Mucinous borderline tumors (n=2)	1	1
Dysgerminoma (n=2)	2	
Mixed germ cell tumor (n=1)	1	
Immature teratoma (n=1)	0	1
Granulosa cell tumor (n=2)	2	

Table 3: Correlation of cytological diagnosis with histopathological diagnosis in ovarian lesions

Histopathology	FNAC		
	Malignant	Benign	Total
Malignant	27	5	32
Benign	1	59	60
Total	**28**	**64**	**92**

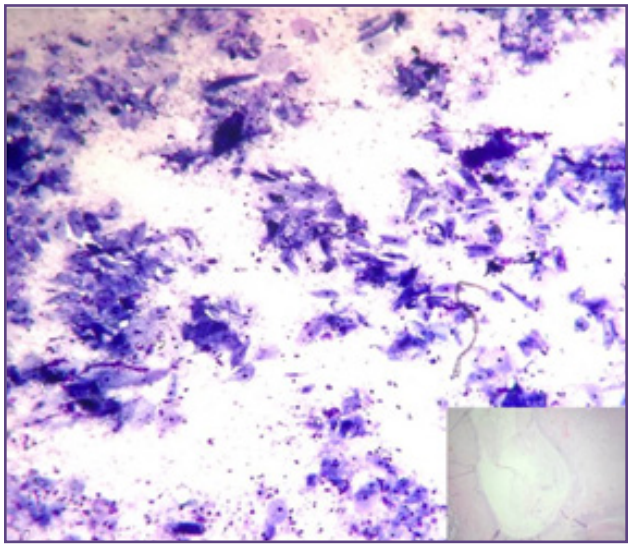

Fig. 1: Benign cystic teratoma; benign squamous cells against a dirty background of keratinous debris (MGG-100X) with inset showing cyst lined by keratinizing suamous epithelial cells (H and E-100X).

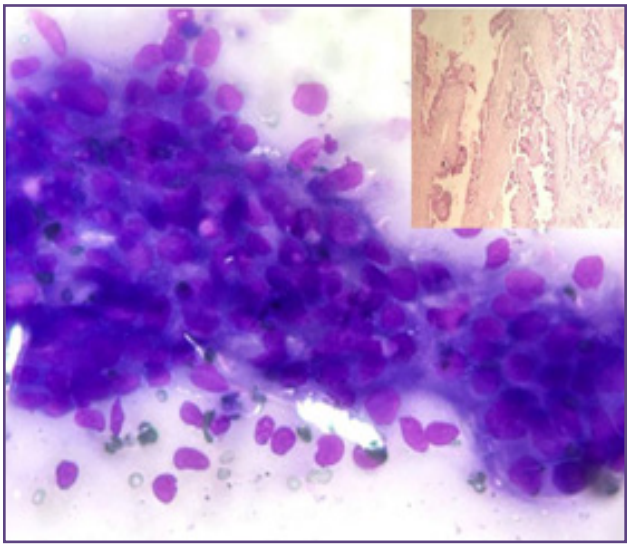

Fig. 2: Papillary fragments lined by malignant glandular cells.(MGG 400X)Inset shows histopathology withcomplex papillary structures lined by anaplastic cells along with stromal invasion.(H and E 100X).

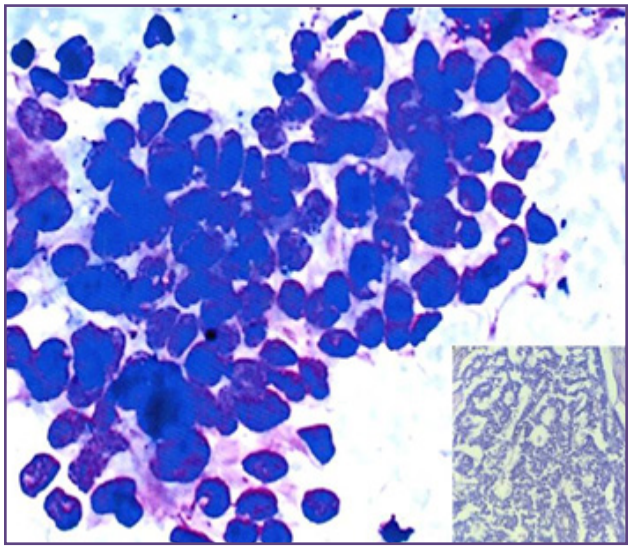

Fig. 3: Granulosa cell tumor;sheetsof monomorphic cells with increased nucleo- cytoplasmic ratio and nuclei with finely granular chromatin forming microfollicular pattern.(MGG-400X) Inset shows histopathology sections monomorphic cells forming Call-Exner bodies (H and E -100X).

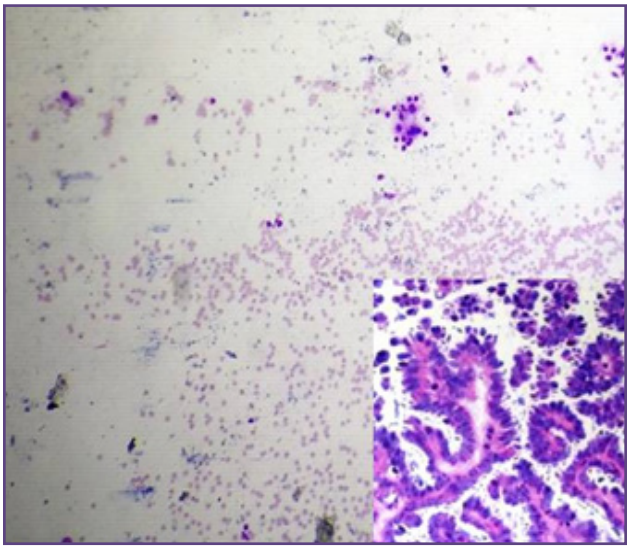

Fig. 4: Scanty cellularity in case of borderline serous tumor showing scattered groups of small epithelial cells with mild nuclear atypia. (MGG-100X) Inset showing histopathology of borderline serous tumor with hierarichal pattern of papillae lined by atypical cells. (H and E -400X).

Discussion

Aspiration cytology has been widely used for both primary diagnosis of ovarian lesions and the follow up of recurrent malignancies. Developing radiologic guidance techniques have also contributed to the higher accuracy of FNAC in recent years. [8]

Due to complexity of lesions and wide spectrum of diagnoses, the cytological diagnosis of ovarian lesions is a challenging process. However, by careful evaluation of the cytoarchitecture and background features, the differentiation into benign and malignant lesions is still possible. [2] In many cases, the pinpoint diagnosis can also be made. The critical issue of this procedure is that FNAC can lead to rupture and spillage of tumor cells into peritoneal cavity and can potentially cause upstaging of malignant tumor. [7]

The magnitude of rise of tumor spillage is unknown and not substantiated by convincing evidence as most of the malignant ovarian tumors present in an advanced stage, the threat of tumor dissemination seems less important when weighed against the effective and economical diagnostic tool available in the form of FNAC. [4]

The sensitivity and specificity of cytology in the diagnosis of ovarian masses in our study was 84.3% and 98.3% with overall diagnostic accuracy of 93.4%. Our observation corroborate closely with other investigations, indicating that FNAC can have appreciable sensitivity, specificity and accuracy in the diagnosis of ovarian masses. Gupta and Rajwanshi found a sensitivity of 85.7% and a specificity of 98.0%. [9] Cole and co workers found FNAC to be highly specific (100%) but conversely with a very low sensitivity of 50%. [10] Ganjei et al and Roy et al in their study found sensitivity and specificity of cytology in diagnosis of ovarian lesions as 94.2%, 91.4%, and 75% , 100% respectively. [11,12]Nazoora et al reported sensitivity of 79.25%, specificity of 90.6% and overall diagnostic accuracy of 89.9%. [13]

The overall diagnostic accuracy in this study was 92.8% compared to overall diagnostic accuracy of 96% described by Moran et al. [14] Wojcik & Selvaggi also reported that the majority of cystic ovarian lesions can be diagnosed accurately; however, they did not correlate FNAC with histology in 53% of their cases. [5]

Several factors may explain the erroneous diagnosis seen in 5 of our cases. Many tumors ovarian cyst fluid may have an inadequate number of cells to accurately assess. Second, malignant cells in an ovary may not be uniformly distributed in the ovary. The number of malignant cells within ovarian cysts may be insufficient or absent to detect with needle aspiration. Tumors of low malignant potential or borderline tumors were difficult to diagnose with accuracy on cytological examination and often could not be clearly distinguished from well-differentiated cystadenocarcinoma or even cystadenomas, as was seen in 3 of our cases. [12,13,15,16] This category of ovarian neoplasms constitutes a grey zone and is subject to inter-observer variations. Histopathology is a pre-requisite for assessing the presence or absence of stromal invasion and for the sub-typing of a tumor as borderline. [1]

Only one false positive result was reported in our study and thus have a high positive predictive value. However, among benign tumours only, one case of Sclerosing tumour Stromal tumour was falsely reported to be suspicious of malignancy on cytology as it showed atypical oval to spindle cells along with formation of Call Exner bodies like structures. Similar findings were also reported by other authors. [17] Moreover, radiological findings in this tumour were suggestive of malignancy because of both cystic and solid areas. Other researchers have also reported incapability of USG and CT in identifying this particular tumour as benign .[18]

Our study and the view of other experts suggest that FNAC is more specific than sensitive in detecting ovarian malignancy and therefore, its use, as a reliable initial diagnostic test, cannot be overemphasized. The cytopathologists should be aware of the potential diagnostic pitfalls and the interpretational errors that can be reduced further, if the aspirates are obtained from different portions of the mass with the use of proper radiological guidance,with expert cytopathologists to perform and interpret the aspirates, and with the use of immunohistochemical and molecular markers.

Conclusion

To conclude the image guided FNAC despite the potential disadvantages, when combined with the available, clinical, radiological and laboratory findings, is a quick, easy, fairly sensitive, specific and cost effective modality for the preoperative diagnosis of malignant as well as benign ovarian masses with minimal morbidity. Accurately identifying borderline tumours and false negative cytological analysis due to low cellularity or secondary degenerative changes may be its limitations but it has high positive predictive value.

Abbreviations

CT - Computed Tomography

FNAC - Fine Needle Aspiration Cytology

USG - Ultrasound

Acknowledgements
None

Funding
None

Competing Interests
None Declared

Reference
1. Goel S, Agarwal D, Goel N, Naim M, Khan T, Ekrammulah. Ultrasound Guided Fine Needle Aspiration Cytology In Ovarian Neoplasms: An Assessment Of Diagnostic Accuracy And Efficacy And Role In Clinical Management. Int J Pathol 2010;11(2):1-6.
2. Uguz A, Ersoz C, Bolat F, Gokdemir A, Vardar MA. Fine needle aspiration cytology of ovarian lesions. Acta Cytol 2005;49:144–8.
3. Hajdu S, Melamed MR. Limitations of aspiration cytology in the diagnosis of primary neoplasms. Acta cytol 1984;28:337-45.
4. Ray S, Gangopadhyay M, Bandyopadhyay A, Majumdar K, Chaudhury N. USG guided FNAC of ovarian mass lesions: A cyto-histopathological correlation, with emphasis on its role in pre-operative management guidelines. J Turk Ger Gynecol Assoc 2014; 15(1):6–12.
5. Wojcik EM, Selvaggi SM. Fine needle aspiration cytology of cystic ovarian lesions. Diagn Cytopathol1994;11:9-14.
6. Geier GR, Strecker JR. Aspiration Cytology and E2 content in ovarian tumors. Acta Cytol 1981;25:400-6.
7. Kreuzer GF, Paradowski T, Wurche KD, Flenker H. Neoplastic or Nonneoplastic ovarian cyst? The role of cytology. Acta Cytol 1995;39:882–6.
8. Mehdi G, Maheshwari V, Afzal S, Ansari HA, Ansari M. Image guided fine needle aspiration cytology of ovarian tumors: An assessment of diagnostic efficacy. J Cytol 2010;27(3):91-5.
9. Gupta N, Rajwanshi A, Dhaliwal LK, Khandelwal N, Dey P, Srinivasan R, Nijhawan R. Fine needle aspiration cytology in ovarian lesions: an institutional experience of 584 cases. Cytopathology 2012;23:300–7.
10. Cole L, Mount S, Nuzzo E, Wong C. Aspiration cytology of ovarian cystic masses: histologic correlation and review of the literature. Acta Cytol 2011;55:19–25.
11. Ganjei P, Dickinson B, Harrison TA, Nassiri M, Lu Y. Aspiration cytology of neoplastic and non-neoplasic ovarian cysts: Is it accurate? Int J Pathol1996;15:94–101.
12. Roy M, Bhattacharya A, Roy A, et al. Fine needle aspiration cytology of ovarian neoplasms. J Cytol 2003;20:31–5.
13. Khan N, Afroz N, Aqil B, Khan T, Ahmad I. Neoplastic and nonneoplastic ovarian masses: Diagnosis on cytology J Cytol 2009;26(4):129–33.
14. Moran O, Menczer J, Gijlad BB, Lipitz S, Goor E. Cytologic examination of ovarian cyst fluid for the distinction between benign and malignant tumors. Obstet Gynecol 1993;82:444–6.
15. Nadji M, Greening SE, Sevin BU. Fine needle aspiration cytology in gynaecologic oncology II, morphologic aspects. Acta Cytol 1979;23:380-8.
16. Kjellgren O, Angstrom T, Bergman F. Fine needle aspiration biopsy in diagnosis and classification of ovarian carcinoma. Cancer1971;28:967-76.
17. Banik T, Gupta N, Rajwanshi A, Dhaliwal LK. Fine Needle Aspiration Cytology in Sclerosing Stromal Tumour of Ovary. A series of 3 cases. Diagnostic Cytopathology 2012:40(4); 342-5.
18. Joja I, Okuno K, Tsunode M et al. Sclerosing Stromal Tumour of Ovary. US, MR and Dynamic MR Findings. J Comput Assist Tomo 2001: 25(2);201-6.