

FNAC: Is it Useful in Diagnosis and Classification of Ovarian Lesions?

POOJA KALA, MONIKA RATHI, ATUL GUPTA, POOJA AGARWAL, HIMANSHUL MOHAN KALA

ABSTRACT

Introduction: Although, infrequently used, Fine Needle Aspiration Cytology (FNAC) is a safe and quite helpful investigation in diagnosing as well as classifying ovarian lesions.

Objectives: Our aim was to assess the efficacy of fine needle aspiration cytology in diagnosis and subsequent classification of ovarian masses.

Material and Methods: This was a prospective study of 83 fine needle aspirates of ovarian masses in females, undertaken under image-guidance from November 2009 through October 2011. We tried to assess the adequacy rates, render cytodiagnosis and then correlate with histology whenever possible.

Results: Adequacy rates were 97.6%. Of 81 adequate cases, 3 were non-neoplastic, 2 benign (including 1

mature teratoma & 1 fibroma), 2 serous borderline tumour and remaining 74 were malignant on FNAC. Among the malignant tumours of ovary, most frequently diagnosed were epithelial tumours (65.2%) followed by germ cell tumours (15.6%). Correlation with histological diagnosis was done. The diagnostic accuracy of FNAC was 89.7%. Sensitivity and specificity were 100% and 80%, respectively. No significant complications were observed.

Conclusion: Fine needle aspiration cytology of ovarian lesions is an accurate, useful and safe diagnostic procedure. It also enables a fairly satisfactory classification of ovarian tumours and thereby facilitates the choice of appropriate therapy.

Keywords: Fine Needle Aspiration Cytology, Ovarian masses, Ovarian tumours

INTRODUCTION

FNAC is less often used for the diagnosis of ovarian tumours by clinicians. FNA of the ovary is generally reserved for cystic masses that by sonographic or laparoscopic examination appear to be benign. Aspiration of radiographically malignant ovarian masses is avoided except to confirm malignancy in patients with inoperable or metastatic disease. There is a risk, albeit slight, of tumour seeding into peritoneal cavity [1]. In patients with solid ovarian lesions, preoperative aspiration cytology may provide important information as to the type of tumour and whether it is benign or malignant, thus aiding the clinician in selecting the appropriate mode of therapy [2]. Considering the not so good prognosis of epithelial ovarian cancer, early evaluation of ovarian lesions becomes important. Kjellgren and Angstrom [3] pointed out that a preoperative cytological assessment allows individualization of treatment, particularly the preoperative irradiation of anaplastic carcinoma. We attempted to diagnose and classify ovarian lesions. Subsequent correlation with histology was done.

MATERIALS AND METHODS

This was a prospective study conducted in a tertiary care centre. Before conducting the study, permission from the

Institutional Ethical Committee was obtained. A total of 83 patients, who were advised fine needle aspiration cytology (FNAC) by Surgery and Gynaecology Departments, were selected for the study from November 2009 through October 2011. Patients with coagulopathy were excluded from the study. A written, informed consent was obtained from patients. Under aseptic precautions, FNAC was done using 22 G needle and 20 mL syringe (Becton Dickinsin, Haryana, India) under the ultrasonographic guidance. The aspirated material was spread on the clean glass slides and smears were prepared. Whenever ascites was associated, ascitic fluid was also sampled after FNAC to look for any spillage during the procedure. Air dried smears were fixed in methanol for 20 - 30 minutes, then stained with May - Grunwald Giemsa stain (BioLab Diagnostics, Mumbai, India). Wet fixed smears were stained by papanicolaou stain.

Detailed clinical, serological and radiological data was obtained, when available. Diagnosis on FNAC was attempted and was compared with histology (accepted as gold standard). World Health Organization (WHO) classification was followed [4].

RESULTS

A total of 83 cases were subjected to FNAC. Age range

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Type of lesion	L	No. of cases	%	
Inadequate (2.4%)		2	2.4%	
Non-neoplastic	Acute bacte	1	1.2%	
(3.6%)	Tub	2	2.4%	
Benign (2.4%)	Mature cy	1	1.2%	
	Fi	1	1.2%	
Borderline tumour (2.4%)	Serous bo	rderline tumour	2	2.4%
Malignant (89.2%)	Epithelial tumours (65.2%)	Serous adenocarcinoma	33	39.9%
		Mucinous adenocarcinoma	6	7.2%
	-	Endometroid carcinoma	6	7.2%
		Clear cell carcinoma	4	4.9%
		Unclassified adenocarcinoma	5	6.0%
	Sex-cord and stromal tumours (3.6%)	Granulosa cell tumour	2	2.4%
		Fibrosarcoma	1	1.2%
	Germ cell tumours (15.6%)	Dysgerminoma	7	8.4%
		Yolk sac tumour	3	3.6%
		Teratoma (2 immature)	2	2.4%
		Mixed germ cell tumour	1	1.2%
	Lymphoma	Large cell lymphoma	1	1.2%
	Metastasis	Metastatic mucinous adenocarcinoma	1	1.2%
	Miscellaneous	Primitive Neuroectodermal tumour (PNET)	1	1.2%
		Small cell carcinoma	1	1.2%
	83	100%		

varied from 15-76 years. The frequency of ovarian lesions was highest in 5th and 6th decade. The number of cases was roughly equal in 2nd, 3rd and 4th decades (12-14.5%). Clinically, lower abdominal/pelvic swelling and pain were the most common complaints. In late second and third decades, germ cell tumours were the most common. On the other hand, surface epithelial tumours commonly affected 4th, 5th and 6th decades. Sex cord-stromal tumours were encountered in 4th, 5th and 2nd decades, equally. Right ovary (62.8%) was found to be more frequently affected. Ultrasonographic evaluation of the 83 ovarian masses revealed 36 solid lesions 38 solid-cystic lesions and 9 cystic ovarian lesions.

Aspirates were considered adequate if the cellular elements were sufficient for rendering diagnosis. Adequate aspirates were obtained in 81 of 83 cases (97.6%). The breakup of 81 cases which were adequate enough for giving a conclusive / suspicious diagnosis on fine needle aspiration is given in [Table/Fig-1].

Aspirate from acute bacterial inflammation revealed numerous neutrophils, few histiocytes and fair numbers of coccal aggregates. Two cases of tuberculosis revealed mainly necrosis. Stain for acid fast bacilli was positive.

For the epithelial neoplasms, the accuracy of FNAC was

87.8%. Aspirates from serous borderline tumour revealed moderately cellular smears with cells predominantly in clusters and forming occasional papillaroid structure. Cells were cuboidal in shape with finely granular nuclear chromatin and only mild nuclear pleomorphism. N/C ratio was focally high.

Aspirates from serous adenocarcinoma showed moderate to abundant (majority) cellularity which was easily identifiable as malignant and as papillary in type [Table/Fig-2] Dark, basophilic, rounded psammoma bodies were seen in 15% cases. Intranuclear cytoplasmic inclusions were seen in 6% cases.

Aspirates from mucinous cystadenocarcinoma (six cases) showed variable cellularity. Cells were present in sheets, singly scattered, focally showing honey comb pattern and picket fencing [Table/Fig-3]. Cells had high N/C ratio, moderate nuclear pleomorphism, nuclear hyperchromasia, fine granular chromatin and distinct nucleolus. Cytoplasm was often well defined, with prominent vacuolization. Mucin was present intracellularly as well extracellularly.

Endometrioid carcinoma on FNAC revealed markedly cellular smears with cells present in prominent acinar pattern, sheets and infrequent papillae. Cells had high N/C ratio, scant pale cytoplasm, hyperchromatic nuclei with granular chromatin,

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[Table/Fig-2]: Serous adenocarcinoma (FNAC) showing papillary aggregate of moderately pleomorphic cells with prominent nucleoli (MGG,400X). [Table/Fig-3]: Mucinous adenocarcinoma (FNAC) showing epithelial aggregates with moderate atypia in a necrotic and mucinous background (MGG,100X). [Table/Fig-4]: Clear cell carcinoma(FNAC): cells with well-defined, clear cytoplasm in a tigroid background. (MGG,400X). (Images from left to right)



cells with bluish cytoplasm, "garland-like" peripheral vacuoles and nuclei with prominent nucleoli (MGG,400X). **[Table/Fig-6]:** Yolk sac tumour (FNAC): poorly differentiated areas mimicking embryonal carcinoma/adenocarcinoma with a suggestion of acini (MGG,400X). (Images from left to right)

irregular nuclear membrane and prominent nucleoli. Nuclear moulding was seen focally. Multinucleation, bizzare nuclei and mitotic activity were also discernible.

Aspirates from clear cell carcinoma [Table/Fig-4] showed high cellularity with tigroid (80% cases) or pink granular (in 20% cases) background. Cells showed papillae formation, acini formation as well as sheets. Cells had distinct cell borders, pale, moderate cytoplasm with cytoplasmic clearing, granularity and vacuolization. Nuclei were oval to round, moderately pleomorphic, hyperchromatic and had granular chromatin and distinct nucleoli. Mitoses and intranuclear cytoplasmic inclusions were variably present. Extracellular eosinophilic basement membrane-like material and blood vessel fragments were also seen. Signet-ring cells, hobnail cells and binucleate forms were also seen. Many large bare nuclei with nucleoli were seen in the background. Cell aggregates with hyalinized core ("Raspberry bodies") were seen.

Five cases were diagnosed as adenocarcinoma, unclassified as these cases could not be further subcategorized on FNAC.

One case was diagnosed as metastatic adenocarcinoma. The cytology revealed highly cellular smear with a mildly hemorrhagic background. Mainly dispersed cells with focal acinar pattern and intracytoplasmic mucin were present. Karyorrhectic debris was also noted. Patient was a known case of primary large bowel malignancy.

All germ cell tumours were accurately classified on FNAC, accuracy rate being 100%. Markedly cellular smears of dysgerminoma [Table/Fig-5] showed predominantly dispersed large round cells with moderate, pale basophilic cytoplasm with peripheral vacuolization. These vacuoles when present, often encircled the nucleus in a garland-like pattern. Nuclei were round, mildly pleomorphic with 1 or 2 prominent nucleoli (Occasionally, macronucleoli). Cytoplasmic as well as nuclear fragility was present in all cases. Numerous bare nuclei were seen in the background. Background was tigroid with fair number of lymphocytes, many plasma cells, few histiocytes and scattered epithelioid cells. Granulomas were also noted in 57.1% cases.

Cytologically, markedly cellular smears of yolk sac tumour [Table/Fig-6] revealed cells in sheets, occasionally forming papillae (representing Schiller- Duval bodies) and acini. These large cells with moderate, pale blue, ill-defined cytoplasm were present in syncytium. N/C ratio was high and nuclei were oval, moderately pleomorphic and had prominent nucleoli, Cytoplasmic vacuolization and characteristic intracytoplasmic as well as extracellular hyaline globules were present invariably. Eosinophillic extracellular basement membranelike material, blood vessel fragments and myxoid background were also present. Aspirate from mature cystic teratoma showed fair number of enucleate squames. Cytology of one case of immature teratoma revealed highly cellular smear in a myxoid background with focal necrosis and haemorrhage. Ectodermal component was represented by anucleate as well as keratinized intermediate and basal squamous cells. Columnar cells in an acinar pattern represented endodermal component. Mesodermal component was represented by adipose tissue. Cytology of second case of immature teratoma revealed small round cells with a tendency to form rosettes. Background comprised of neuropil-like material and focal necrosis. These cytological features were suggestive of immature teratoma with a predominance of neuroectodermal components. One case was diagnosed as small round cell tumour, most likely primitive neuroectodermal tumour. Smears were extremely cellular and comprised dispersed as well as

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Tumour type	Cytodiagnosis	Histology available in no. of cases	Positive cyto- histological correlation & %	Misdiagnosed cases
Surface epithelial tumours	Serous borderline tumour	2/2	2 (100%)	0
	Serous adenocarcinoma	28/33	25(89.3%)	2→Serous borderline tumour 1→Endometriod adenocarcinoma
	Mucinous adenocarcinoma	5/6	5(100%)	0
	Endometrioid adenocarcinoma	4/6	4(100%)	0
	Adenocarcinoma unclassified	2/5	0	2→metastatic adenocarcinoma
Germ cell tumours	Dysgerminoma	7/7	7(100%)	0
	Dermoid cyst	1/1	1(100%)	0
	Immature teratoma	2/2	2(100%)	0
	Yolk sac tumour	2/3	2(100)	0
Sex cord- stromal tumours	Granulosa cell tumour	2/2	2(100%)	0
	Fibroma	1/1	1(100%)	0
	Fibrosarcoma	1/1	0(0%)	1→cellular fibroma
	Metastatic adenocarcinoma	1/1	1(100%)	0
Total		58	52 (89.7%)	6(10.3%)

aggregated, mitotically active small round cells with scanty cytoplasm, nuclei with granular chromatin and inconspicuous nucleoli. Rosettes were seen focally. Few spindled nuclei were also noted. Apoptotic bodies were also seen. There was a distinct suggestion of neuropil in the background at places. No lymphoglandular bodies were seen. Cytology was entirely consistent with a malignant small round cell neoplasm with features suggestive of PNET or neuroblastoma. However, the adolescent age group and absence of an adrenal or paraspinal mass rendered the possibility of neuroblastoma most unlikely. Hence, a diagnosis of PNET was rendered. Aspirate from mixed germ cell tumour comprised of two population of cells with features of immature teratoma and dysgerminoma respectively.

The diagnostic accuracy for the sex cord-stromal tumour was 80%. Aspirates from granulosa cell tumour revealed cellular smears. Cells were not only present singly, but also formed follicular pattern, occasional papillae and pseudopapillae (i.e. perivascular arrangement of the cells) in a clean background. Almost monomorphic, medium sized cells had scant to moderate ill-defined pale cytoplasm with some small, punctate vacuoles. Nuclei were round with fine granular chromatin and discernible nucleoli. Nuclear grooves were noted in a small proportion of cells. Prominent blood vessel fragments and extracellular hyaline globules were also noted. Aspirate from fibroma revealed scantly cellular smears with monomorphic spindle cells having bland nuclei, present singly and in loosely cohesive clusters. Cytological diagnosis of fibrosarcoma was made on the basis of moderately cellular smears comprising of fascicles and singly lying moderately pleomorphic spindle cells with occasional nucleoli and some nuclear membrane irregularity in a hemorrhagic background. On histopathology, the tumour was diagnosed as cellular fibroma.

One case was diagnosed as small cell carcinoma. Highly cellular smears revealed predominantly dispersed, small cells with occasional acinar formation. The cells were minimally pleomorphic, had scant basophilic cytoplasm, a high N/C ratio, granular chromatin, inconspicuous nucleoli and discernible mitosis. Nuclear moulding was also a feature. Background showed necrosis, some hemorrhage and inflammation. Apoptotic bodies were numerous. Clinical details were helpful in the diagnosis, i.e. age of the patient (36 years) and liver metastasis. Small cell carcinoma of hypercalcemic type is the most common form of undifferentiated carcinoma of the ovary in the females under 40 years of age. Spread beyond ovary is usual [5]. Diagnosis of large cell Non Hodgkin lymphoma, ovary was reliably made on FNAC in view of its characteristic cytological features.

Cytological diagnosis was compared with histopathological diagnosis in 58 cases. Out of these, 52 (89.7%) cases were correctly diagnosed on cytology [Table/Fig-7] The discordant cases included-two serous borderline tumours

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misdiagnosed as serous adenocarcinoma, one endometrioid adenocarcinoma misdiagnosed as serous adenocarcinoma, one cellular fibroma misdiagnosed as fibrosarcoma and two of the adenocarcinoma, unclassified turned out to be metastatic. Ascitic fluid analysis was possible in 28 cases (33.7%). None of these revealed significant tumour spillage into the peritoneal cavity post-FNAC.

Considering FNAC as diagnostic tool under evaluation and histology as gold standard diagnostic modality in the diagnosis and classification of ovarian tumours with special reference to post-pubertal age group, following values were calculated.

Diagnostic accuracy= 89.7%

Sensitivity=100%

Specificity=80%

Positive predictive value=98.1%

Negative predictive value=100%

On follow-up for a year, no complication related to seeding of tumour into peritoneal cavity was noted in any case. Overall, no significant complications (except minimal discomfort & pain at the time of needle puncture) were observed in the current study.

DISCUSSION

The adequacy rate achieved in the present series was 97.6%. Nadji et al., [6] and Dey et al., [7] commented on adequacy rates in aspirates from whole female genital tract in their studies i.e. 98.5% and 98.7%, respectively.

Accuracy of FNAC in differentiating benign and malignant gynaecological tumours was reported by Ganjei et al., [8]to be 94.5%. Hemlatha et al., [9] reported accuracy of imagedirected percutaneous FNAC to be 89.9% and a false negative rate of 4.76%. In the present study, all FNAC were image directed and the accuracy was 89.7%. False negative rate was 0%. Papathanasiou et al., [10] commented that sensitivity and specificity of FNAC in cystic lesions of ovary were 25% and 97%, respectively. Sensitivity rate of image-guided FNAC in diagnosing ovarian tumours as documented by Bandyopadhyay et al., [11] was 100%. In present study, sensitivity and specificity rates were 100% and 80%.

In the present study, majority lesions were malignant (91.4%) In previous studies, malignant lesions constituted 18-62% [12-16] of all cases. The difference can be due to the fact that in our set-up, FNAC of ovarian masses was limited to those cases, where ultrasonography showed a solid or solid-cystic tumour or features suggestive of malignancy. After considering this fact, the results of current study were comparable to the previous studies. Image-directed FNAC is quite useful for diagnosis of solid ovarian tumours [11].

Although FNAC can reliably classify most of the ovarian lesions, but differentiation between endometrioid carcinoma and serous cystadenocarcinoma, serous borderline tumour and serous adenocacinoma, fibrosarcoma and cellular fibroma can be problematic. We could diagnose 50% of

serous borderline tumour on FNAC. Athanassiadou reported the FNAC of borderline neoplasms [17]. Gupta et al., reported fibrosarcoma as one of the discordant cases in their study [18].

Not all adenocarcinomas could be classified on cytology. We had five such cases in current study. Two of these cases were diagnosed as metastatic adenocarcinoma on histopathology. Khan et al., [19] commented that a metastatic adenocarcinoma was misdiagnosed as serous cystadenocarcinoma on cytology in their study. Possibility of a metastatic deposit should be considered in the differential diagnosis of a malignant epithelial neoplasm of ovary on FNAC.

Besides, it is difficult to categorise a granulosa cell tumour as juvenile or adult type. Only a few isolated case studies are available describing the features of juvenile granulosa cell tumour [20,21]. Three dimensional clusters, rosettes, loose monolayers and individual cells; Call-Exner bodies, pseudopapillae, presence of nuclear grooves and vacuolated cytoplasm suggest granulosa cell tumour of adult type. While monolayered, loosely cohesive sheets, single cells; nuclear pleomorphism with clefting and protrusions, paucity of nuclear grooves and Call-Exner bodies, frequent mitosis and finely granular cytoplasm with numerous vacuoles suggest granulosa cell tumour, juvenile type [20]. Cytodiagnosis of small cell carcinoma and primitive neuroectodermal tumour was challenging. Clinico-radio-pathological correlation is helpful in such cases. Uguz et al., also suggested that clinical, radiological, laboratory and cytological should be utilised for accurate diagnosis on FNAC [15].

LIMITATION

In the present study, no significant complication was observed. This confirms the similar findings in earlier study [11]. Seeding into peritoneal cavity can be prevented by using thin bore needle and avoiding multiple passes during aspiration.

Image-directed FNAC is a safe, rapid, easy and reliable diagnostic modality in the management of ovarian lesions especially neoplasms. It can help in the early pre-operative diagnosis of ovarian neoplasm and help clinician to plan the further management. It is especially useful in cases where reproductive ability of the patient needs to be preserved. Fairly satisfactory classification can be achieved on FNAC.

CONCLUSION

Fine needle aspiration cytology of ovarian lesions through image guidance is an accurate, useful and safe diagnostic procedure, which enables diagnosis with fair degree of ease without resorting to major surgery merely for diagnostic purposes. The method also enables a fairly satisfactory classification of ovarian tumours and thereby facilitates the choice of appropriate therapy. Thus fine needle aspiration cytology has significant role in the diagnosis of ovarian lesions, but must be employed less hesitantly.

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AUTHOR(S):

- 1. Dr. Pooja Kala
- 2. Dr. Monika Rathi
- 3. Dr. Atul Gupta
- 4. Dr. Pooja Agarwal
- 5. Dr. Himanshul Mohan Kala

PARTICULARS OF CONTRIBUTORS:

- 1. Demonstrator, Department of Pathology, AlIMS, Rishikesh, Uttarakhand, India.
- 2. Junior resident, S.N. Medical college, Agra, UP, India.
- 3. Professor and Head, Department of Pathology, S.N. Medical college, Agra, UP, India.
- 4. Lecturer, Department of Pathology, S.N. Medical College, Agra, UP, India.

5. Senior Resident, Department of Otorhinolaryngology, HIMS, Dehradun, UK, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Pooja Kala,

C/O Dr Dinesh Mohan Kala,

5- New Road, Opposite Doon Hospital, Dehradun-248001, Uttarakhand, India.

E-mail : poojahimanshul@gmail.com

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