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Original Research Article

Fine Needle Aspiration Cytology of Neoplastic and Nonneoplastic Ovarian Masses with Histological Correlation

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ABSTRACT

Background: Efficacy and accuracy of image-guided FNAC in the pre-operative diagnosis of ovarian masses depends on various factors. Although, borderline tumors are difficult to diagnosed by this method. However benign and malignant epithelial tumors can be diagnosed accurately.
Aim: The main aim of this study was to assess the sensitivity, specificity and diagnostic accuracy of USG-guided FNAC in neoplastic and non-neoplastic ovarian masses, considering histopathology as the gold standard.
Materials and Methods: A total of 80 patients diagnosed with suspected ovarian masses by clinical and imaging modalities from Jan 2014 to Dec 2015 included in this study. USG guided FNA was performed and diagnosis was established. The cytological diagnosis was confirmed by histopathological examination. Descriptive statistics were used to determine correlation between cytological and histological diagnosis.
Results: On examination of fine needle aspirated material, 12 cases were diagnosed benign non neoplastic cyst. Thirteen cases could not be categorized either due to nonspecific findings or due to inadequate cytological material on aspiration. On histopathological examination all benign cases were diagnosed as benign tumor except one case of mucinous cystadenoma was diagnosed as borderline mucinous cystadenocarcinoma. One case was diagnosed as borderline mucinous adenocarcinoma which turned out mucinous adenocarcinoma on histological examination. Sensitivity, specificity and accuracy of FNAC were 82.3%, 92.3% and 84.2% respectively.
Conclusion: Image assisted FNAC is rapid and fairly accurate procedure for the diagnosis of ovarian masses with high sensitivity and specificity. With careful cytological examination all the ovarian masses can be categorized into benign and malignant lesion which can decrease unnecessary surgical morbidity.

Keywords: ovarian masses, fine needle aspiration, Histological correlation, diagnostic accuracy.

INTRODUCTION

Ovarian mass in advanced age is a matter of concern, due to the increased risk of malignancy in this age group. The majority of ovarian masses are benign which can occur in both young and old age woman but malignant ovarian tumors present at mostly in advanced stage. Non-conclusive diagnosis of current diagnostic techniques might be the cause of unnecessary surgical morbidity. [1,2] Fine-needle aspiration cytology (FNAC) provides some advantages for evaluating ovarian masses due to excellent patient compliance and low complication rate. [3] However, borderline tumors and false negative cytological analysis are high on cytology examination due to low cellularity or

secondary degenerative changes. [1,2] If all types of ovarian masses are analyzed in sufficient numbers by FNAC, it might improve the diagnostic accuracy. Possibility of seeding of tumor during FNA procedure has been documented. The magnitude of risk of such a procedure is unknown and not substantiated by convincing evidence. [4,5]

Image-guided FNAC is a quick method with high sensitivity and specificity and cost effective procedure for the preoperative diagnosis of ovarian masses with minimal morbidity. It may help in avoiding unnecessary surgical morbidity and making decisions regarding neoadjuvant chemotherapy; because most of ovarian malignancies present at late stage. [6-8]

Although histopathological examinations remain the gold standard for diagnosis of ovarian masses, previous studies have attempted to estimate the accuracy of image-guided FNAC in pre-operative diagnosis of ovarian masses. [9-17] The main aim of this study was to assess the sensitivity, specificity and diagnostic accuracy of USG-guided FNAC in neoplastic and non-neoplastic ovarian masses, considering histopathology as the gold standard.

MATERIALS AND METHODS

Present study was conducted from January 2014 to December 2015. A total of 80 patients diagnosed with suspected ovarian masses by clinical examination (abdominal and per vaginal examination) and/or by imaging modalities such as USG were included in the study during this period. These patients were evaluated by transabdominal percutaneous FNA approach under USG guidance. The mass was localized and aspiration performed using a 22-to 23-gauge needle attached to a 20 ml syringe. For deep-seated masses, a lumbar puncture needle was used.

Aspirated material was immediately smeared on glass slides. Two air dried smears prepared for Leishman/Giemsa stain. Two wet fixed smears fixed in 95% alcohol were stained by Papanicolaou stain. Records of clinical and radiological data as well as serum tumor markers (cancer antigen 125 and alpha fetoprotein) wherever available, were recorded for diagnostic correlation. The smears were evaluated for the following cytological features: cellularity, arrangement of cells, features of epithelial cells, foamy / hemosiderin-laden macrophages, background material (proteinaceous, granular, greasy or mucoid). Based on cytomorphology, the lesions were classified as (1) nonneoplastic benign cysts, (2) benign neoplasms and (3) malignant neoplasms.

The results were compared with the histopathology diagnosis accepted as the gold standard. Special stains (immunomarker, PAS, etc) were employed as and when required. In cases where cyst fluid was aspirated, sediment was obtained from cytocentrifugation and was stained by similar methods. Descriptive statistics were used to determine correlation between cytological and histological diagnosis. Sensitivity and specificity for the cytological diagnoses were calculated using the histological confirmation as the gold standard.

RESULTS

Table 1: Age distribution of patients with suspected ovarian masses

Age groups	No. of cases	Percentage
11-20	1	1.2%
21-30	4	5%
31-40	19	23.8%
41-50	13	16.3%
51-60	22	27.5%
61-70	14	17.5%
71-80	6	7.5%
81-90	1	1.2%
Total	**80**	**100%**

Present study include a total of 80 patients with age range vary between 11 to 87 years and mean age of 53 years. (Table 1) The majority of patients with ovarian masses presented in the third to sixth decade of life, with a peak in the fifth decade (n=22). Clinically, most of the patients presented with abdominal swelling, pain and menstrual disturbances. Assessment of the type of lesion (whether solid or cystic), size,

location and extent of the lesion was done by ultrasonography.

On examination of fine needle aspirated material, 12 cases were diagnosed benign nonneoplastic cyst, which were not categorized further. Thirteen cases could not be categorized either due to nonspecific findings or due to inadequate cytological material on aspiration. The benign neoplasm comprised of serous cystadenoma (02 cases), mucinous cystadenoma (04 cases), benign cystic teratoma (01), and granulosa cell tumor (1 case). The granulose cell tumor had cellular smear consisting of small sized malignant cells with nuclear grooves and scanty amount of cytoplasm. In serous cystadenoma, straw colored fluid was aspirated and smears were scant cellular. A few papillary aggregates of the bland epithelial cells were seen along with foamy macrophages and few inflammatory cells. In cases of mucinous cystadenomas, tall columnar cells with basally displaced nuclei and vacuolated cytoplasm in some were observed against a mucinous background. On histopathological examination all benign cases were diagnosed as benign tumor except one case of mucinous cystadenoma which was diagnosed as borderline mucinous cystadenocarcinoma. One case diagnosed as borderline mucinous adenocarcinoma turned out is mucinous adenocarcinoma on histological examination. (Table 2)

Out of 80 cases, blood was aspirated on FNA in 6 cases. Out of these, surgical specimen was received in 3 cases, which were diagnosed as leiomyoma, mucinous adenocarcinoma and fibrothecoma. Out of 7 cases which were labeled as inadequate on cytological examination, 2 cases were diagnosed as granulosa cell tumor and mucinous adenocarcinoma. In 5 cases, surgical specimens were not received. Three cases were labelled as positive for malignancy due to lack of specific features. These were diagnosed as serous adenocarcinoma (2 cases) and borderline serous adenocarcinoma (1 case) on histological examination.

Table 2: Cytological diagnosis on FNA smears in ovarian masses

Diagnosis	No. of cases	percentage
Benign	12	15%
Blood	6	7.5%
Inadequate	7	8.8%
Non-conclusive (neoplasm)	3	3.6%
Serous cystadenoma	2	2.5%
Mucinous cystadenoma	4	5%
Borderline Mucinous adenocarcinoma	1	1.2%
Serous adenocarcinoma	18	22.5%
Mucinous adenocarcinoma	16	20%
Granulosa cell tumor	1	1.2%
Poorly differentiated carcinoma	9	11.5%
Teratoma	1	1.2%
Total	**80**	**100%**

Table 3: Comparison of cytological and histopathological diagnosis in ovarian masses

Cytological examination		Histopathological examination		
Diagnosis	**No of cases**	**Specimen received**	**Diagnosis**	
Benign	12	-	-	-
Blood	6	3	1	leiomyoma
			1	Mucinous cystadenoma
			1	fibrothecoma
Inadequate	7	2	1	Granulosa cell tumor
			1	Mucinous adenocarcinoma
Non-conclusive- positive neoplasm	3	3	2	serous adenocarcinoma
			1	Borderline serous adenocarcinoma
Serous cystadenoma	2	2	2	Serous cystadenoma
Mucinous cystadenoma	4	4	3	Mucinous cystadenoma
			1	Borderline Mucinous adenocarcinoma
Borderline Mucinous adenocarcinoma	1	1	1	Mucinous adenocarcinoma
Serous adenocarcinoma	18	8	7	Serous adenocarcinoma
			1	Borderline Serous adenocarcinoma
Mucinous adenocarcinoma	16	4	4	Mucinous adenocarcinoma
Granulosa cell tumor	1	-	-	-
Poorly differentiated carcinoma	9	4	3	Serous adenocarcinoma
			1	Mucinous adenocarcinoma
Teratoma	1	-	-	-
Total	**80**	**31**		

The smears of malignant papillary serous cystadenocarcinoma were hypercellular with papillary aggregates of malignant epithelial cells having large hyperchromatic nuclei and high nuclear-cytoplasmic (N/C) ratio. Sheets and papillary aggregates of columnar mucin-producing cells with malignant features in background of mucin were highly suggestive of mucinous cystadenocarcinoma. Eighteen cases were labelled as serous adenocarcinoma on cytological examination. Out of these we received specimen in 8 cases. Seven cases diagnosed with same result, however one case lack features of invasion and labeled as borderline serous adenocarcinoma. Sixteen cases were diagnosed mucinous adenocarcinoma on cytological features. Only 4 specimens were received for histopathological confirmation and diagnosed as mucinous adenocarcinoma. Nine cases were diagnosed as poorly differentiated carcinoma due to lack of features specific to any tumor and absence of supporting immunohistochemical staining results. We received surgical specimen in four cases. Out of these four cases, 3 were diagnosed as mucinous adenocarcinoma and one was serous adenocarcinoma. (Table 3) Sensitivity, specificity and accuracy of FNAC were 82.3%, 92.3% and 84.2% respectively.

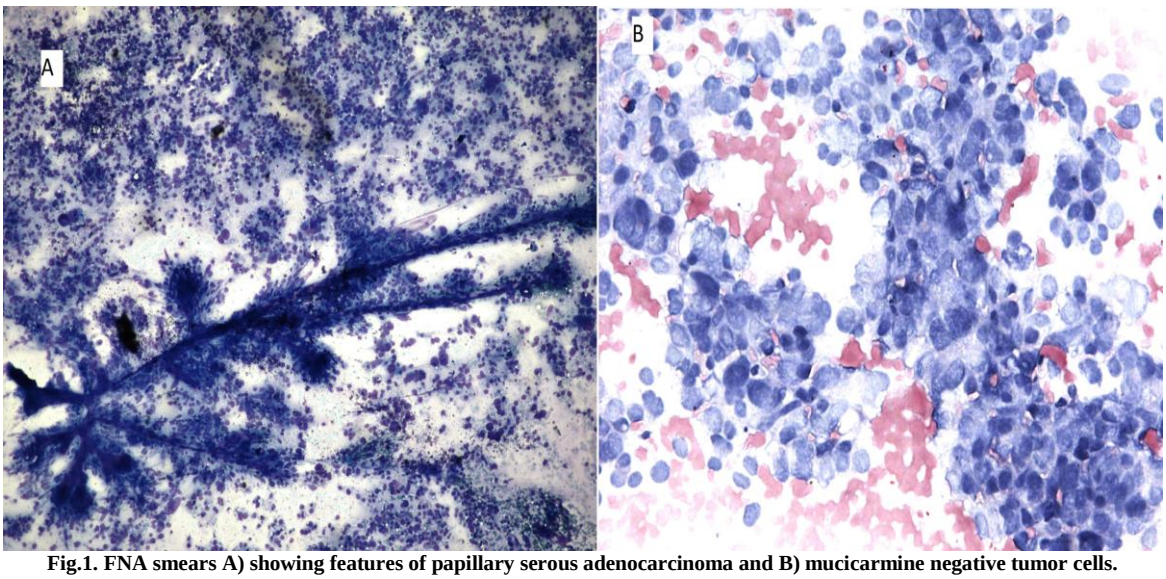

Fig.1. FNA smears A) showing features of papillary serous adenocarcinoma and B) mucicarmine negative tumor cells.

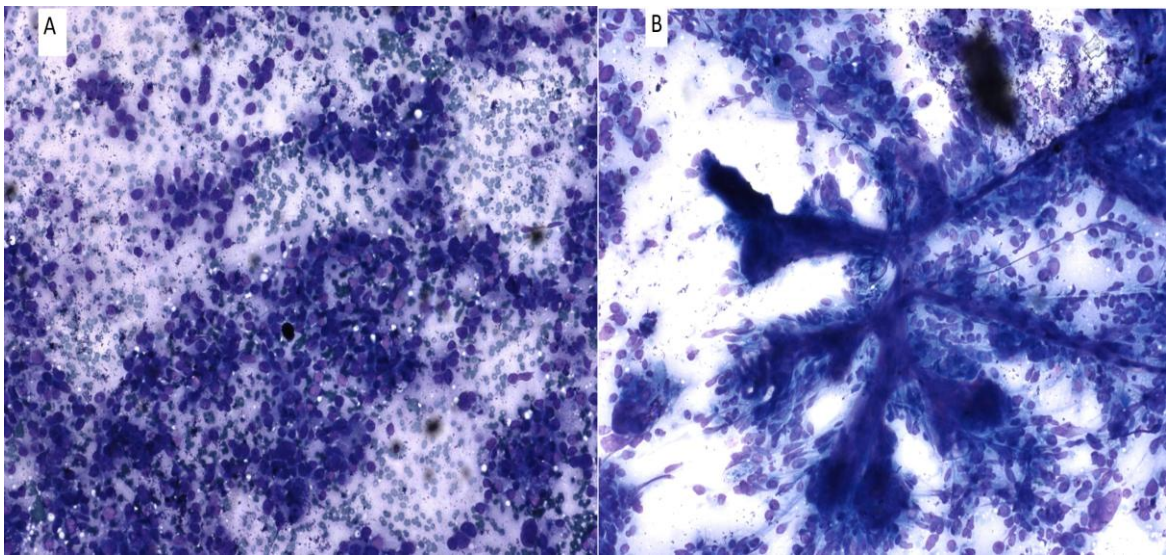

Fig.2. FNA smear A) and B) revealing features of mucinous adenocarcinoma.

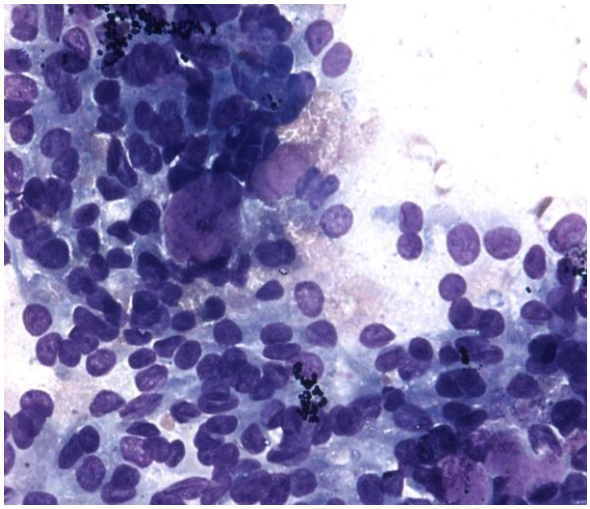

Fig.3. FNA smear showing cytomorphological features of granulosa cell tumors

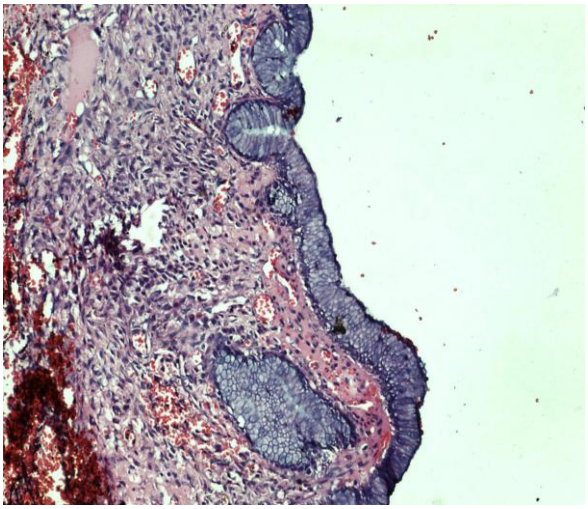

Fig.5. H&E stained sections showing nonciliated cells columnar cells with basal nuclei and abundant intracellular mucin (mucinous cystadenoma).

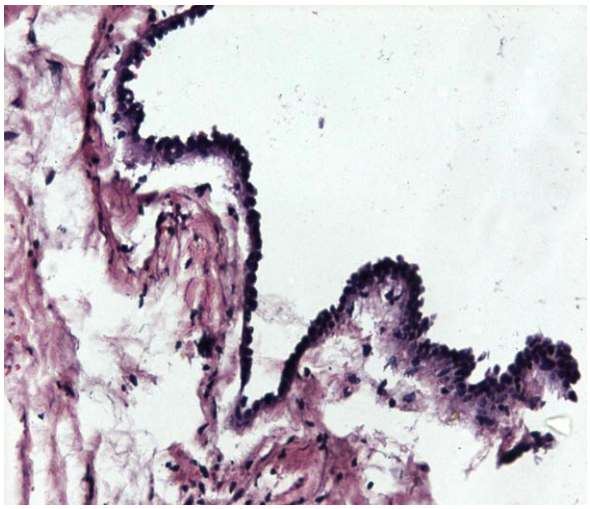

Fig.4. H&E stained sections showing cuboidal non-ciliated epithelium with tumor stroma (serous cystadenoma).

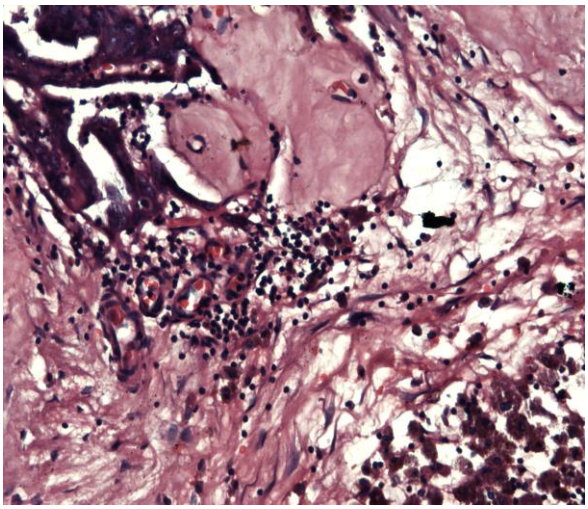

Fig.6. H&E stained sections showing focal area of papillary adenocarcinoma with collection of hemosiderin laden macrophages (previous FNA site).

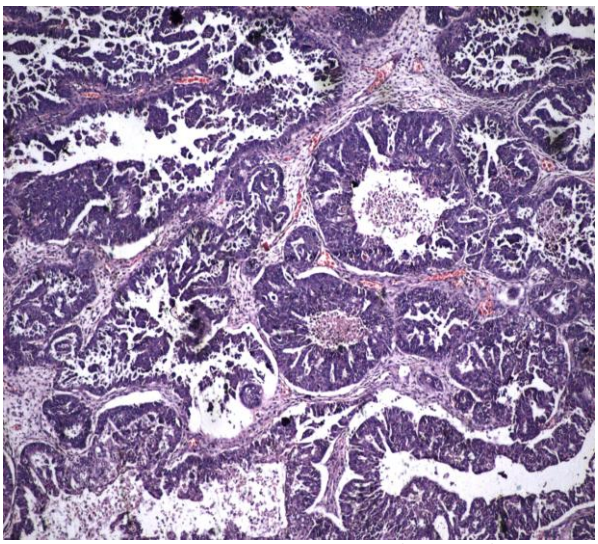

Fig.7. H&E stained sections showing histomorphological features of serous adenocarcinoma.

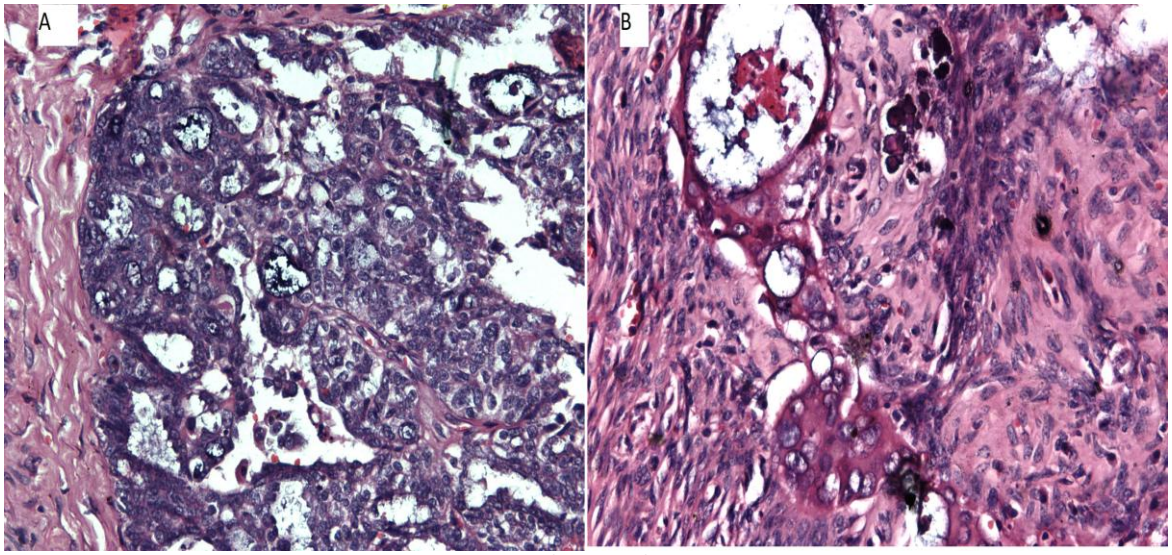

Fig.8. A) H&E stained sections showing histomorphological features of mucinous adenocarcinoma, and B) H&E stained sections showing tumor foci with psammoma bodies.

DISCUSSION

There are conflicting results regarding the diagnostic accuracy of FNA in ovarian masses. New advanced radiologic guidance techniques have also contributed to the higher accuracy of FNAC in recent years. FNAC has been used both for primary diagnosis and follow-up in malignant ovarian lesions due to higher accuracy. Due to complex cytological features and the wide spectrum of diagnostic category, cytological analysis of ovarian lesions is a difficult issue. [8]

Borderline tumors were difficult to diagnose on cytological examination and often falsely diagnosed in well-differentiated cystadenocarcinoma or even benign cystadenomas. This category of ovarian neoplasms constitutes a grey zone due to higher inter-observer variations. In borderline tumor, histopathology is a necessary for identification of the presence or absence of stromal invasion. A high index of suspicion and careful evaluation of cytological features is therefore essential for diagnosis of borderline tumor. [1,2]

Out of 80 cases, in 31 cases we received excised ovarian masses for histopathological examination. On histopathological examination all benign tumor cases were diagnosed as benign except one case of mucinous cystadenoma was diagnosed as borderline mucinous cystadenocarcinoma. One case was diagnosed as borderline mucinous adenocarcinoma which turned out mucinous adenocarcinoma on histological examination. One case out of 8 cases of serous adenocarcinoma was diagnosed as borderline malignancy on histology. In Various studies, borderline malignancy was most common category which leads false positive and negative results on cytological examination. Sensitivity, specificity and accuracy of FNAC were 82.3%, 92.3% and 84.2% respectively.

In study of Khan N et al, out of 38 cases of serous cystadenoma, eight cases proved to be false negative mainly due to scanty and degenerated cell material. Four cases out of 12 (mucinous cystadenoma) proved to be false negative due to the presence of thick mucoid material obscuring the cellular details. There were three false-positive cases in the malignant category, one case each of borderline serous cystadenocarcinoma, mucinous cystadenocarcinoma and metastatic carcinoma, all falsely interpreted as serous cystadenocarcinoma, while one case was wrongly diagnosed as mucinous cystadenoma owing to the lack of clear-cut malignant features and abundant mucin in the background. Thus, the sensitivity and specificity of cytology in the diagnosis of a

variety of ovarian masses was 79.2% and 90.6%, respectively. [13]

Cytological diagnosis was rendered on all the 42 ovarian lesions, with a correct diagnosis in 34 cases, resulting in a diagnostic accuracy of 80.9% in study of Mehdi G at al. Most of the cases with discordant diagnoses were surface epithelial tumors of low malignant potential and required histopathological examination for a final diagnosis. Three cases of serous and 2 cases of mucinous cystadenocarcinomas of low malignant potential could not be identified correctly on cytological examination. [14]

Bandyopadhyay A et al also found discordant in cytological and histological examination of ovarian masses. Out of 10 benign serous cystadenomas, 8 showed the same histopathological diagnosis, but 2 came out to be borderline serous tumors. Among the cytologically diagnosed six mucinous cystadenomas, all correlated well with histopathology. Out of 18 cases diagnosed as serous adenocarcinoma, 15 cases had concordant histopathological diagnosis, 2 cases were of borderline malignancy in histopathology and a single case was reported as undifferentiated carcinoma. Among the nine cytological diagnoses of mucinous adenocarcinoma, only one proved to be a case of Krukenberg tumor and another one was borderline mucinous tumor and the rest of seven cases correlated well. [15]

Gupta N et al examined a total of 584 cytological smears of ovarian masses. Of the 584 lesions, 180 (30.8%) were reported as nonneoplastic, 249 (42.6%) as neoplastic (81 benign lesions/tumors and 168 malignant) and 155 (26.5%) as inadequate. Based on the subsequent histopathology, which was available in 121 (20.7%), the cases were divided into those that were concordant and discordant. Concordant cases comprised 92/121 (76%) and discordant cases comprised 29/121 (24%). Out of these discordant cases, 14 surface epithelial tumors including one cystadenofibroma, one borderline mucinous tumor and 12 carcinomas were result in discrepancy with histopathological examination. FNAC sensitivity for a diagnosis of malignancy was 85.7%, specificity 98.0%, positive predictive value 97.7%, and negative predictive value 87.7%. [16]

In study of Ray S et al, cytological diagnosis was obtained in all 83 ovarian lesions: 56 cases were benign, 6 possibly benign, 3 suspicious of malignancy and 18 cases were malignant. Two cases of borderline mucinous tumor, 1 case of borderline serous tumor and 1 mucinous cystadenocarcinoma were diagnosed erroneously in their study in cytology. Thus, the sensitivity of cytological diagnosis was 83%, and specificity was 97%. [17]

The conflicting results on in accuracy of cytological evaluation of ovarian masses may be due to differences in the technique used to aspirate the lesion as well as differences in smear preparation. Lack of informative clinical parameters of the patients may be important, including serum markers and USG findings. Several other factors may explain a poor cyto-histopathological correlation. Ovarian cyst fluid may have occasional atypical cells along with or without foamy macrophages which cannot give an accurate impression of the lesion. In addition, borderline epithelial tumors are difficult to interpret on aspiration cytology.

CONCLUSION

One of the major limitations for the use of FNAC in ovarian tumors is the high percentage of inadequate samples. Sometime the aspirate may represent peritoneal rather than cystic fluid due to incorrect localization of lesion. False-negative results of FNAC in ovarian cystic lesions especially in borderline malignancy are usually due to the low cellularity and secondary degenerative changes. Clinical examination, pelvic ultrasound and FNAC were complementary diagnostic techniques in ovarian masses and none of the methods was diagnostic by themselves. Therefore, all

clinical and sonographic findings should be considered in collaboration with cytological findings for definite diagnosis. FNAC has a high specificity and accuracy for diagnosis of ovarian masses and sensitivity is limited by inconclusive/inadequate results.

Conflict of interest: All authors state that there are no conflicts of interests.

REFERENCES

1. Cibas ES. Ovary. In: Cibas ES, Ducatman BS, editors. Cytology Diagnostic Principles and Clinical Correlates. 4th ed. New York, USA: Saunders; 2003.p.406.
2. Koss LG. Tumors of the Ovary and Fallopian Tube. In: Koss LG, Melamed, editors. Koss' Diagnostic Cytology and its Histopathologic Bases. 5th ed. New York, USA: Lippincott Williams & Wilkins; 2006.p.493.
3. 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.
4. Higgins RV, Matkins JF, Marroum MC. Comparison of fine-needle aspiration cytologic findings of ovarian cysts with ovarian histologic findings. Am J Obstet Gynecol. 1999; 180:550-3.
5. Uguz A, Ersoz C, Bolat F, Gokdemir A, Vardar MA. Fine needle aspiration cytology of ovarian lesions. Acta Cytol 2005; 49:144-8.
6. Martinez‐Onsurbe P, Ruiz Villaespesa A, Sanz Anquela JM, Valenzuela Ruiz PL. Aspiration cytology of 147 adnexal cysts with histologic correlation. Acta Cytol. 2001; 45:941-7.
7. Athanassiadou P, Grapsa D. Fine needle aspiration of borderline ovarian lesions: Is it useful? Acta Cytol. 2005; 49:278-85.
8. Spencer JA. A multidisciplinary approach to ovarian cancer at diagnosis. Br J Radiol. 2005; 78:S94-S102.
9. Ganjei P. Fine‐needle aspiration cytology of the ovary. Clin Lab Med. 1995; 15:705-26.
10. Ahmad SS, Akhtar K, Akhtar S, Abrari A, Nasir A, Khalid M, et al. Ultrasound guided fine needle aspiration biopsy of abdominal masses. JK Science. 2006; 8:200-4.
11. Sood T, Handa U, Mohan H, Goel P. Evaluation of aspiration cytology of ovarian masses with histopathological correlation. Cytopathology. 2010; 21:176-85.
12. Hemalatha AL, Divya P, Mamatha R. Image-directed percutaneous FNAC of ovarian neoplasms. Indian J Pathol Microbiol. 2005; 48:305-9.
13. Khan N, Afroz N, Aqil B, Khan T, Ahmad I. Neoplastic and nonneoplastic ovarian masses: Diagnosis on cytology. Cytol. 2009; 26(4):129-33.
14. 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.
15. Bandyopadhyay A, Chakraborty J, Chowdhury AR, Bhattacharya A, Bhattachrya P, Chowdhury MK. Fine needle aspiration cytology of ovarian tumors with histological correlation. J Cytol. 2012; 29:35-40.
16. Gupta N, Rajwanshi A, Dhaliwal LK, Khandelwal N, Dey P, Srinivasan R, et al. Fine needle aspiration cytology in ovarian lesions: an institutional experience of 584 cases. Cytopathology. 2012; 23:300-7.
17. 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.

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