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Diagnostic utility of imprint cytology of ovarian neoplasm: A cyto-histological comparison

Reily Ann Ivan[1], Kuruvilla P Chacko[2,*], Blessy Mary Thomas[1]

[1]*Dept. of Pathology, Believers Church Medical College, Thiruvalla, Kerala, India*
[2]*Dept. of Obstetrics and Gynecology, Believers Church Medical College, Thiruvalla, Kerala, India*

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ABSTRACT

Background: Intra-operative cytology (IOC) is a method of intra-operative pathological evaluation of cytology smears. The most important indication for IOC is to establish or confirm diagnosis rapidly. Other advantages of IOC are its simple, inexpensive, excellent preservation of cellular details, with no loss of tissues as occurs with cryostat sections and adequacy of surgical margins. Frozen sections are well established method for providing rapid and accurate intra-operative diagnosis.
Objective: To evaluate the diagnostic utility of imprint cytology and assess the accuracy of imprint cytology with histopathological diagnosis obtained from ovarian neoplasm.
Materials and Methods: Imprint smears were prepared immediately from all the ovariotomy specimens. The specimens were sent for histopathology along with prepared smears to categorize as benign, borderline and malignant. Sensitivity, specificity and accuracy were assessed.
Results : Among the 99 specimens studied, 80 were benign, 9 borderline and 10 malignancy according to histopathology. We found that sensitivity, specificity, for benign lesions were 100%, 42.1% and for malignant lesions were 80%, 91.9% respectively. The overall accuracy was 89%.
Conclusion : Imprint smear of ovarian neoplasm gives a rapid diagnosis with 89% accuracy against histopathology with added advantages. Imprint cytology is an adjunct to frozen section for providing an intra-operative diagnosis; however, in resource poor settings, it can be used as a stand-alone method for aiding intra-operative decision making.

1. Introduction

Ovarian cancer is the fourth most frequent cause of cancer death in women and accounts for 5% of all cancer deaths. Intra-operative cytology (IOC) is increasingly being employed as a method of intra-operative consultation. In ovarian lesions, IOC has been reported to have comparable diagnostic accuracy to frozen sections. The most important indication for the IOC is to establish or confirm diagnosis rapidly. Different authors[1,2] have reported several advantages of IOC such as:

1. Preparation with preserved accuracy in rapid;
2. Easy and economical method;
3. Preservation of cellular details without freezing artefacts;
4. Reduction in tissue loss;
5. Potential detection of crucial neoplastic lesions or variable elements in large tissue fragments;
6. Can be performed even limited tissue is available; and
7. Negligible contamination with safe handling[3]

Cytological evaluation of imprints and smears should be considered an important complementary tool in the setting of intra-operative consultation.[4–6] Ovarian specimens are very commonly submitted for intra-operative consultation in order to confirm the presence of malignancy.[7] Borderline mucinous tumours comprised the single largest source of error in frozen section.[8,9] Among the several cytological

* *Corresponding author*.
E-mail address: kuruvillapayyampallilchacko@gmail.com. (K. P. Chacko).

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techniques applied to ovarian specimens, scrape cytology is often considered the most suitable.[2] The description of the imprint smears of fresh tissues in the rapid microscopic diagnosis of tumours are the milestone in the development.[10]

Cytological specimens may be obtained using needle sampling of resected surgical specimens (bench aspirates) by direct touch imprints, or by scraping and smearing cellular materials from the cut surface of the tumour onto the slides. Fine needle aspiration cytology (FNAC) in the preoperative investigation of ovarian tumours has been discouraged since the puncture of a cystic carcinoma might cause intra-peritoneal seeding, but IOC enables a rapid diagnosis without fear of dissemination of ovarian cancer.[11] Cytological evaluation is also superior to frozen sections in the diagnosis of select types of ovarian neoplasms, but in general frozen section diagnosis is reported to be more accurate and sensitive than that of cytological smears alone, and the latter should play mostly a very useful complementary role.[12] To keep this is mind, an attempt was made to evaluate the diagnostic utility of imprint cytology and assess the accuracy of imprint cytology with histopathological diagnosis obtained from ovarian neoplasm.

2. Materials and Methods

This was a hospital based prospective cross-sectional study done from May 2018 to November 2019 in Believers Church Medical College, Kerala, India. Permission for this study was obtained from the institutional review committee. All ovarian tumours including cysts were received fresh in normal saline and the process for imprint cytology was done on the same day thereby gross findings were noted. Ultrasonography findings and tumour markers were recorded.

Imprint and squash smears were taken from all ovarian tumours from surgically removed specimens which were sent to the pathology department for frozen section and histopathological examination. Specimen was then cut open with a sharp knife. Samples for imprint cytology were obtained from several parts of the tumours presenting different gross morphology, and the samples underwent Papanicolaou staining. These slides were examined immediately and reported as benign or malignant.

Surgical resection tissues fixed in 10% formalin were routinely processed for light microscopy, and the histological diagnosis of the tissue sections was made by H.E. staining. The histological diagnosis of an ovarian tumour was established according to a newly published WHO classification.[13] Total time taken for smear preparation; staining and reporting was about 15 minutes. The diagnosis of scrape cytology was compared with final histopathological diagnosis.

3. Results

The present study consisted of 99 cases. The age ranged from 21 to 74 years. The final histopathological diagnosis showed that 80, 9 and 10 were benign, borderline and malignant respectively. Distribution of various histological types of ovarian neoplasm in our study is shown inTable 1. The correlations between the imprint smear diagnosis and final histopathology are shown in Table 2. The overall diagnostic accuracy of intraoperative imprint cytology has been satisfactory, with those of 89% of the cases correlating with the final diagnosis.

The diagnostic value of imprint smear according to the status of malignancy in terms of sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) is shown in Table 3. Eleven of the study cases in which intra-operative imprint cytology did not correlate with the final diagnosis and their descriptions of misdiagnosed were reported and tabulated (Table 4).

The scrape technique was found to be the best method for preparing the smears. Cellularity was high compared to other techniques and morphological preservation was also better. Rapid papanicolaou staining was found at par in quality with the routine technique. It took only 2 minutes 30 seconds and was able to show good cytoplasmic nuclear differentiation as well as matrix material. Average time taken to provide a diagnosis was found to be about 15 minutes from removal of specimens.

4. Discussion

In our study, sensitivity, specificity, positive predictive value and negative predictive value for benign lesions were 100%, 42.1%, 87.9%, 100% and for malignant lesions were 80%, 91.9%, 100%, 97.8% respectively. The overall accuracy was 88.9%. The accuracy in diagnosing borderline tumours was very low. This is similar to another study where imprint cytology of 55 cases were examined of benign, borderline and malignant.[1,11,14] The benignity and malignancy were diagnosed entirely by imprint cytology. The diagnostic accuracy of borderline tumours was very low in that study.[14]

The intra-operative diagnosis of borderline tumours by cytology is difficult because of admixture of benign and borderline areas in the same tumour and evaluation of stromal invasion not possible by cytology. In our study, nine cases of borderline tumours were underdiagnosed to benign entities where another study was recorded with 6 cases.[11,15] The review suggested that borderline tumours cannot be more accurately diagnosed by intra-operative cytology when borderline malignant areas are the main component of tumour.[15] The present study involved a small number of borderline tumours-serous, mucinous and endometrioid tumours. On histopathology stratification with mild atypia was seen and reported as borderline mucinous tumor.[16]

Table 1: Distribution of various histological types of ovarian neoplasm in our study

No.	Ovarian Neoplasm	Imprint	Histopathology
1	**Serous tumour**		
	Benign	36 (36.4)	33 (33.4)
	Borderline	0	3 (3.0)
	Malignant	4 (4.0)	4 (4.0)
2	**Mucinous tumour**		
	Benign	12 (12.1)	8 (8.1)
	Borderline	0	4 (4.0)
	Malignant	2 (2.0)	2 (2.0)
3	**Endometrioid tumour**		
	Benign	2 (2.0)	0
	Borderline	0	2 (2.0)
4	**Clear cell carcinoma**	1 (1.0)	1 (1.0)
5	**Granulosa cell tumour**	1 (1.0)	0
6	**Fibroma**	5 (5.1)	5 (5.1)
7	**Fibrosarcoma**	1 (1.0)	1 (1.0)
8	**Immature teratoma**	0	1 (1.0)
9	**Mature teratoma**	18 (18.2)	16 (16.2)
10	**Struma ovarii**	1 (1.0)	2 (2.0)
11	**Carcinoid**	0	1 (1.0)
12	**Endometriotic cyst**	16 (16.2)	16 (16.2)
	Total	99 (100)	99 (100)

Table 2: Comparison of imprint smear diagnosis with histopathological diagnosis according to malignant status

Imprint Smear	Histopathology			
	Benign	Borderline	Malignant	Total
Benign	80 (87.9)	9 (9.9)	2 (2.2)	91 (100)
Borderline	-	-	-	-
Malignant	-	-	8 (100)	8 (100)
Total	80 (80.8)	9 (9.1)	10 (10.1)	99 (100)

Table 3: Diagnostic value of imprint smear according to the status of malignancy in terms of sensitivity, specificity, PPV and NPV

Statistical Value (%)	Benign (%)	Borderline (%)	Malignant (%)
Sensitivity	100	0	80
Specificity	42.1	100	91.9
PPV	87.9	-	100
NPV	100	90.9	97.8
Overall Accuracy		88.9	

Table 4: Unmatched imprint smear diagnosis

Imprint Smear	Histopathology	Number
Benign Serous Tumour	Borderline Serous Tumour	2
Benign Mucinous Tumour	Borderline Mucinous Tumour	4
Benign Endometrioid	Borderline Endometrioid	2
Granulosa Cell Tumour	Carcinoid	1
Mature Teratoma	Immature Teratoma	1
	Struma Ovarii	1

Amid with various cytological techniques applied to ovarian specimens, scrape cytology is often considered the most suitable.[11,17,18] In our study also, we experienced FNAC from the tumor and imprints from the cut surface of tumor, scrape, and crush cytology is very much useful to maximize the cell harvest. The comparison of intraoperative cytology and frozen sections in the present study indicates that imprint cytology is superior to frozen sections in diagnosing the histological types of carcinoma, such as clear cell carcinoma and mixed carcinoma. Overall, nearly 85% of malignant ovarian tumors are epithelial, which contributes to the superiority of imprint cytology for the diagnosis of these tumours.[14]

Study with a large number of cases with borderline tumours is needed to the application of imprint cytology in borderline tumours. The comparison of imprint/ squash cytology with final histopathology diagnosis indicates that imprint/ squash smears are equally good in diagnosing malignancies of serous, mucinous, clear cell carcinoma and fibrosarcoma while immature teratoma and the carcinoid was wrongly diagnosed. Benign cases can be effectively diagnosed using imprint/ squash cytology. But in case of fibroma, lack of cellularity may cause inability to report and Struma ovarii may be mistaken for teratoma. Overall, through this study, it was identified that the imprint cytology is a cost effective, easy, rapid and consistent method for diagnosis of various ovarian neoplasms.

5. Conclusion

Imprint smear of ovarian neoplasm gives a rapid diagnosis with 89% accuracy against histopathology with added advantages of rapidity of preparation, simple and inexpensive method, preservation of cellular details and minimal contamination with safe handling. For benign and malignant neoplasm imprint cytology is very useful, but in Borderline cases and solid ovarian neoplasm it is not useful.

6. Source of Funding

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7. Conflict of Interest

None.

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Author biography

Reily Ann Ivan Associate Professor

Kuruvilla P Chacko Professor

Blessy Mary Thomas Assistant Professor

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