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Research Article

Imprint cytology in the diagnosis of ovarian lesions

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ABSTRACT

Background: Ovarian neoplasms constitute a major bulk of surgical pathology specimens. Histopathology is the gold standard in diagnosis. Of the many options available for a rapid intra-operative diagnosis imprint cytology has many advantages. This study therefore aimed to study the imprint cytology of ovarian lesions and compare with the histopathology findings and analyze the statistical effectiveness of this study as a rapid intra-operative diagnostic tool.
Methods: 200 lesions resected over a 2 year period were included in the study. Lesions were bisected when fresh. Clean glass slides touched firmly over the representative areas. Immediate fixation was in 95% ethanol and staining was by Rapid Papanicolaou method. Of the 200 cases studied, 5 were lost to follow up, and hence were excluded from the study.
Results: The 195 cases were classified broadly according to WHO system into 4 groups and the lesions were statistically analyzed. 122 surface epithelial tumors showed 97.5%sensitivity and 94.5%specificity in diagnosis with an overall accuracy of 96.4%. 8 sex cord stromal tumors had 98.5% diagnostic accuracy with a specificity of 99.5%. There was 100 % sensitivity and specificity in diagnosing the 25 germ cell tumors. The tumor like lesions showed a diagnostic accuracy of 97% with a specificity of 100%.
Conclusions: Imprint cytology is an inexpensive and a fairly sensitive tool for rapid intra-operative diagnosis.

Keywords: Imprint cytology, Intra-operative diagnosis, Ovarian lesions

INTRODUCTION

Histopathology is the gold standard in diagnosis of resected specimens. Rapid intra-operative opinion is required to stage the disease and to modify the surgical procedure. [1] Many options are available.[2-4] Frozen section is most frequently resorted to. A major bulk of histopathology specimens is comprised of ovarian lesions. Preoperative and rapid intra-operative consultation is often called for.[5-8] In gynecologic surgeries frozen section is not often called for. However there is an increase in the preoperative FNA diagnosis being sought.[5] Knowing the cyto-morphology of ovarian lesions will help in diagnosing lesions on FNA. Imprint cytology, as also scrape cytology offers the advantage of viewing the gross, giving serial cuts, taking multiple, representative samples and most importantly, being inexpensive and logistically un-demanding. This study was undertaken with the following objectives:

1. To study the imprint cytology of ovarian lesions comparing with their histopathology.
2. To evaluate the statistical implications of imprint cytology in diagnosing ovarian lesions.

METHODS

A total of 200 resections of ovarian neoplasms performed in our Gynecology Department over a period of 2 years were included in the study. The lesions were bisected when fresh, serial cuts made, when necessary. The

surface was mopped dry off fluid or blood. Clean and dry glass slides were touched firmly to the cut surface. Representative areas were imprinted. The slides were immediately fixed in 95% ethanol or its equivalent 80% isopropyl alcohol. Staining was by the Rapid Papanicolaou method. The results were compared to histopathology. The statistical parameters studied included: sensitivity, specificity, positive predictive value and overall accuracy of diagnosis. This was done using SPSS method. The calculation was as shown in Table1.

Table 1: Statistical parameters studied.

		Histopathology		
		positive	negative	total
Imprint cytology	Positive	TP (a)	FP(b)	
	Negative	FN(c)	TN(d)	
	total			

Where, TP = true positive, FP = false positive, TN = true negative, FN = false negative
So,
Sensitivity = a/a+c *100
Specificity = d/d+b*100
Positive predictive value = a/a+b*100
And, overall accuracy = a+d/n*100
Where, n = number of lesions studied.

RESULTS

Of the 200 lesions imprinted, 5 were lost to follow up in the department, and hence, were excluded from the study. The 195 cases thus included were broadly categorized according to WHO classification [9] as

1. Surface epithelial stromal tumors
2. Sex cord stromal tumors
3. Germ cell tumors and
4. Miscellaneous

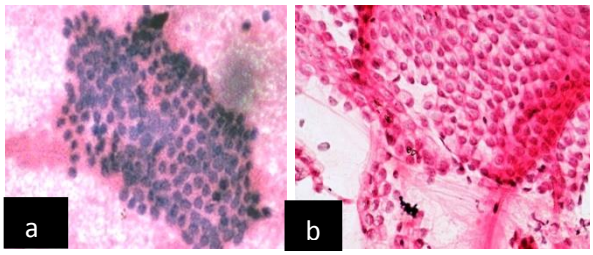

Figure 1: a) imprint smear showing serous cystadenoma with monolayered sheet of cuboidal cells with uniform nucleus (pap, x400). b) mucinous cystadenoma with columnar cells in monolayered sheet showing honey-comb appearance and peripheral palisading (pap, x400).

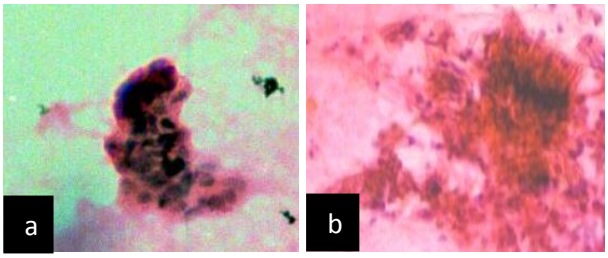

Figure 2: a) borderline serous tumor with cells in papillaroid clusters (Pap, x 400).
b) Borderline mucinous tumor with columnar cells in tight and papillaroid clusters (Pap, x200).

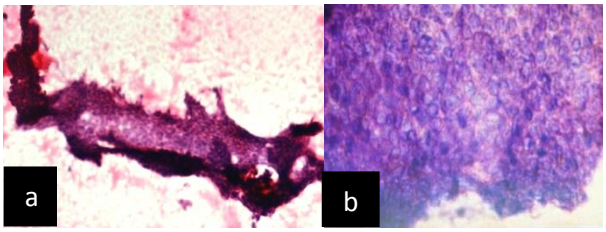

Figure 3: a) serous cystadenocarcinoma showing small cells in branching papillary pattern (Pap, x 200)
b) mucinous cystadenocarcinoma showing columnar cells in three dimensional clusters with nuclear pleomorphism (Pap, x 400).

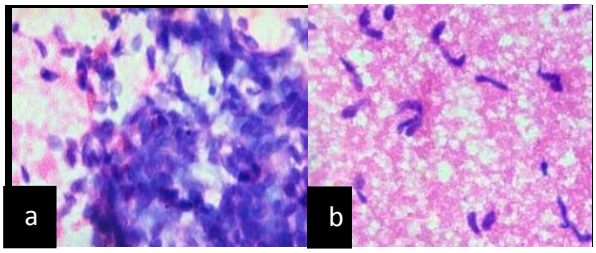

Figure 4: a) granulosa cell tumor showing cells in clusters and microfollicular pattern. The cells have a scanty cytoplasm and nucleus with grooves and nucleoli (Pap, x 400)
b) fibroma-thecoma shows elongated cells in an amorphous background (Pap, x 400).

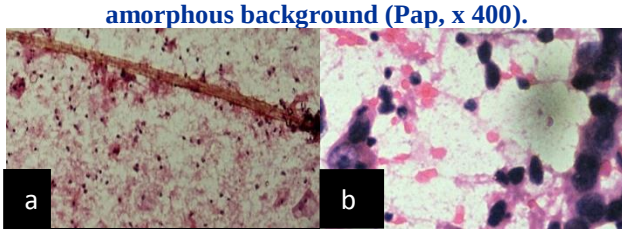

Figure 5: a) mature cystic teratoma showing nucleated squames and hair shaft (Pap, x 200)
b) dysgerminoma with large round cells in discohesive clusters with round nucleus showing prominent nucleoli. Background shows lymphocytes. (Pap, x 400).

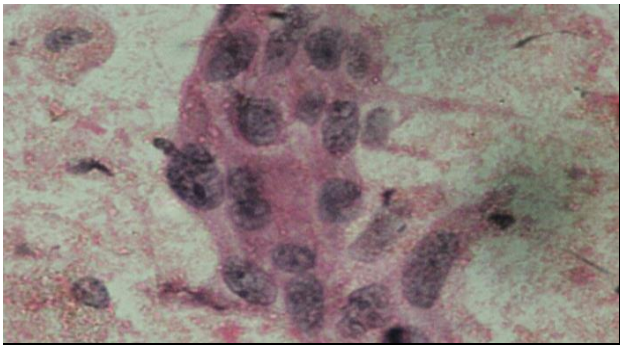

Figure 6: endometriosis with endometrial stromal cells and hemosiderin laden macrophages. (Pap, x 400).

There were 122 surface epithelial tumors. These included, 56 serous, 55 mucinous, 5 endometrioid, and 2 cases of clear cell tumors. Of these, 119 could be correctly interpreted. Of the 8 case of sex cord stromal tumors, 4 cases of fibroma-thecoma and 1 case of granulosa cell tumor could be interpreted correctly. There were 25 cases of germ cell tumors, of which 23 were mature cystic teratomas, and 1 was a dysgerminoma. There were 31 cases of tumor like lesions including endometriotic cyst, follicular cyst etc. There were 9 cases which could not be categorized on imprint and were labeled inconclusive. They could be diagnosed on histology.

DISCUSSION

Preoperative and intra-operative diagnostic cytology is finding increasing use in the present day when the patient care and management has become very individualized. [1] The various methods include Fine Needle Aspiration Cytology, frozen section and imprint smear cytology. Scrape cytology has also been advocated as a comparable tool for rapid diagnosis.[2,8] FNA of both superficial and deep lesions from various sites is an accepted diagnostic modality. However, its use in gynecologic practice has been limited to investigation of suspected pelvic recurrences in patients treated for cancers. Its use in pre-operative and intra-operative diagnosis of ovarian lesions is controversial for the following reasons:

1. Fear of spillage of tumors contents into peritoneal cavity and secondary implantation.[10]
2. Capsule rupture leading to upstaging of the tumor.
3. It is also felt that a preoperative FNA of ovarian lesions may be unnecessary since a surgical exploration is mandatory.

Another problem with FNA of ovarian lesion is the lack of representativeness of sample, especially, in lesions with a variegated appearance and in cystic masses[11-13] with multiple locules. Multiple punctures from multiple sites may be needed. The cellular yield from cystic lesions is low and this can be improved by biochemical analysis of the cyst fluid.[10] Frozen section is a rapid diagnostic tool. However, it requires costly equipments, and more technical expertise.

Imprint smear is another technique which is a simple, rapid and reliable diagnostic modality [14, 15]. Moreover, cellular yield is more with this technique, different sites of the tumor can be assessed and it preserves the architecture better. Another advantage of imprint over FNA is that the gross morphology of the ovarian lesions can be studied in detail while preparing imprint. Imprint smears can be used to study the cytology of ovarian tumors, type them as benign or malignant and, further classify them. They also help in the staging of ovarian tumors studying the cytology of lymph nodes, omentum and peritoneum.[7]

Out of 122 cases of surface epithelial stromal tumors, 119 were correctly diagnosed by imprint. There were 56 serous tumors, 48 benign cyst adenomas, one borderline tumor and 7 cystadenocarcinomas. There were difficulties in interpreting 4 benign cases giving a low accuracy of diagnosis and positive predictive value. Study of the gross was very helpful in diagnosing borderline and malignant cases. Mucinous tumors formed the next large group with 55 cases consisting of 47 benign tumors, 5 borderline tumors and 3 cystadenocarcinomas. Benign and most of the borderline could be diagnosed on cytology but 2 malignant tumors were mistaken as borderline on cytology.[11] 5 cases of endometrioid tumors were obtained in the study material, 4 being endometrioid adenocarcinoma, interpreted correctly on cytology and one was Malignant Mixed Mullerian Tumor which was interpreted as poorly differentiated serous carcinoma. There were two cases of clear cell carcinomas, both of which could be diagnosed by imprint.

Of the 8 cases of sex cord stromal tumors, there were five fibroma-thecomas, one granulosa cell tumor and two Sertoli cell tumors**.**[16] Leiomyoma was in one case misinterpreted as fibroma. Hence, the positive predictive value of diagnosing sex cord stromal tumor on imprint was 85.7%, with a sensitivity and specificity of 75% and 99.5% resp.

Germ cell tumors were the most easily diagnosed lesions due to their classic gross and cytologic picture and included 23 mature cystic teratomas, 1 dysgerminoma and 1 malignant germ cell tumor.[17]

Miscellaneous lesions or the tumor like lesions numbered 31, which included 16 endometriotic cysts. Some of these were interpreted wrongly on cytology.

Table 2 shows the statistical analysis of the various ovarian tumors.

Table 2: Statistical analysis of the 195 ovarian neoplasms according to their WHO classification.

Lesions	Sensitivity	Specificity	Positive predictive value	Accuracy
surface epithelial stromal	97.5%	94.5%	96.7%	96.4%
sex cord-stromal	75%	99.5%	85.7%	98.5%
germ cell tumor	100%	100%	100%	100%
Miscellaneous	80.6%	100%	100%	97%

CONCLUSION

Thus, to conclude, the present study showed 96.4% accuracy in diagnosing surface epithelial lesions, almost 100% accuracy in identifying germ cell tumors and 98.5% accuracy in categorizing sex cord stromal tumors. It had an accuracy of 97% in identifying the various tumor-like lesions. Imprint cytology, though not very specific in all cases, is a very useful diagnostic tool in the intra-operative consultation of ovarian tumors. It is a simple, rapid, inexpensive and reliable technique requiring about 5-10 minutes, when a rapid staining technique is used. It also does not need costly infrastructure or technical expertise and does not have the risk of instrument contamination. So it can be used as an alternative to frozen section as a rapid intra-operative diagnostic tool.

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