



Original Research Article

Role of imprint cytology in the diagnosis of ovarian neoplasms

Archana Shivamurthy^{1,*}, Padmapriya Jaiprakash²¹Dept. of Pathology, JSS Medical College, Mysore, Karnataka, India²Dept. of Pathology, Kasturba Medical College, Manipal University, Manipal, Karnataka

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ABSTRACT

Primary ovarian neoplasms constitute a heterogeneous group of benign and malignant tumors of epithelial, sex cord–stromal, mesenchymal and germ cell origin. Secondary tumors constitute a minority. The management of benign and malignant ovarian neoplasms varies and it is here that imprint cytology plays a crucial role in diagnosis. It provides a rapid intraoperative diagnosis which will decide further treatment course for the patient. Imprint cytology of ovarian neoplasms is simple, inexpensive, challenging and provides a rapid diagnosis with excellent cellular details. The aim of the present study is to determine the role of imprint cytology in the diagnosis of ovarian neoplasms. A retrospective study was conducted in the department of pathology. A total of 53 cases were included in the study. In 48 cases, the imprint cytology findings correlated with the histopathological diagnosis. 5 cases did not correlate. Epithelial ovarian tumors accounted for the majority, (85%) followed by germ cell tumors (9.4%) and sex cord stromal tumors (5.6%). The sensitivity and specificity were 93.75% and 100% respectively. Thus imprint cytology is an effective cytological method in the diagnosis of ovarian neoplasms. Knowledge of specific cytological features for each tumor type helps in accurate diagnosis which in turn is valuable in immediate appropriate treatment and management of patients with benign or malignant neoplasms.

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1. Introduction

Ovarian neoplasms are a diverse group of tumors which exhibit a spectrum of morphological characteristics, clinical manifestations, genetic alterations, and tumor behaviors. This high degree of variability presents a major challenge in both diagnosis and treatment. Imprint cytology provides a rapid intraoperative diagnosis which will decide further treatment course for the patient.^{1–5} It is a simple, inexpensive, challenging and provides a rapid diagnosis with excellent cellular details. Knowledge of both cytological and histopathological features plays a crucial role in accurate diagnosis, which in turn affects patient management. An accurate final histological

diagnosis is important owing to the major differences in incidence, tumor behavior and clinical outcome between each histologic subtype.^{6–11} Hence the aim of the present study is to determine the role of imprint cytology in the diagnosis of ovarian neoplasms

2. Materials and Methods

A retrospective study was conducted at the department of pathology from January 2011 to December 2015 for a period of five years. A total of 53 cases were included in the study. Imprint cytology smears stained with hematoxylin and eosin (H & E) were reviewed along with respective frozen sections and routine histopathology slides. Imprint cytology slides and scrape smears were made immediately from representative solid areas on cut section of the ovarian

* Corresponding author.

E-mail address: archana_018@yahoo.co.in (A. Shivamurthy).

masses which were sent for frozen section analysis. The slides were wet fixed and stained with H & E stain. The distinct cytological features on imprint smears and scrape smears were noted in each case. The diagnosis made on imprint cytology were correlated with the final histopathology diagnosis in each of these cases. The sensitivity, specificity and diagnostic accuracy of the test were calculated. Statistical analysis was made using SPSS v26.

3. Results

A total of 53 cases of ovarian tumors, having imprint smears, frozen section slides and routine histopathology slides were included in the study. The age ranged from 18-78 years. Epithelial ovarian tumors accounted for the majority, (85%) followed by germ cell tumors (9.4%) and sex cord stromal tumors (5.6%).

Table 1: Distribution of ovarian neoplasms

Type of tumor	No of cases	Percentage
Surface epithelial tumors	45	85.0
Sex cord stromal tumors	03	5.6
Germ cell tumors	05	9.4
Total	53	100

Among the surface epithelial cell tumors, serous and mucinous tumors accounted for the majority, most common being serous and mucinous cystadenomas (33.3% each). There were two cases of malignant endometrioid carcinoma and 1 case each of benign endometrioid tumor, benign brenner tumor and clear cell carcinoma.

Sex cord stromal tumors accounted for a minority group in the present study represented by 1 case each of fibroma, fibrothecoma and Sertoli-Leydig cell tumor.

There were 5 cases of germ cell tumors, 2 cases of mature cystic teratoma, 2 cases of dysgerminoma and 1 case of mixed germ cell tumor.

In 48 cases, the imprint cytology findings correlated with the histopathological diagnosis. In 5 cases, imprint cytology findings did not correlate with the final histopathological diagnosis. These were one case of mixed germ cell tumor with yolk sac component and embryonal component, one case of endometrioid carcinoma was misdiagnosed as cystadenocarcinoma, one case of mucinous carcinoma which was misdiagnosed as borderline mucinous tumour and two cases of borderline mucinous tumour which were misdiagnosed as a mucinous cystadenomas. Thus the sensitivity and specificity were 93.75% and 97% respectively.

Table 2: Surface epithelial tumors of ovary

Tumor type	No of cases	Percentage%
Surface epithelial tumors		
Serous tumors:		
Benign (cystadenoma)	15	33.3
Borderline tumors (serous borderline tumor)	2	4.4
Malignant (serous adenocarcinoma)	3	6.6
Mucinous tumors, endocervical-like and intestinal type:		
Benign (cystadenoma)	15	33.3
Borderline tumors (mucinous borderline tumor)	5	11.1
Endometrioid tumors:		
Benign (cystadenoma)	1	2.3
Malignant (endometrioid carcinoma)	2	4.4
Clear cell tumors:		
Malignant (clear cell adenocarcinoma)	1	2.3
Transitional cell tumors:		
Brenner tumor -Benign	1	2.3
Total no of cases	45	100

Table 3: Sex cord stromal tumors

Tumor type	No of cases	Percentage
Sex cord-stromal tumors-Pure stromal tumors		
Fibromas	1	33.4
Fibrothecomas	1	33.3
Sertoli -Leydig cell tumor		
Sertoli-leydig cell tumor	1	33.3
Total no of cases	3	100

Table 4: Germ cell tumors

Tumor type	No of cases	Percentage
Teratomas		
Mature cystic teratoma	2	40
Dysgerminoma	2	40
Mixed germ cell tumor	1	20
Total number of cases	5	100

4. Discussion

Intraoperative evaluation of tumors was mainly done through frozen sections until 1927 when cytology was introduced as one of the methods of intraoperative evaluation by Dudgeon & Patrick.^{12,13} Presently in ovarian lesions, studies have reported that imprint and scrape cytology have diagnostic accuracy comparable to frozen sections with crisp cellular details. Being the eighth most common cancer among women, it includes about 4% of all women's cancers. It has the highest morbidity and mortality rates among cancers of the reproductive system.^{2,4,5,10}

Ovarian neoplasms have extensive heterogeneity both within and between histologic subtypes.^{14,15} In addition to age specific clinical and radiological features, a thorough knowledge of specific cytological features [Table 5,6] of each subtype is crucial to make an accurate diagnosis on imprint cytology and frozen sections.

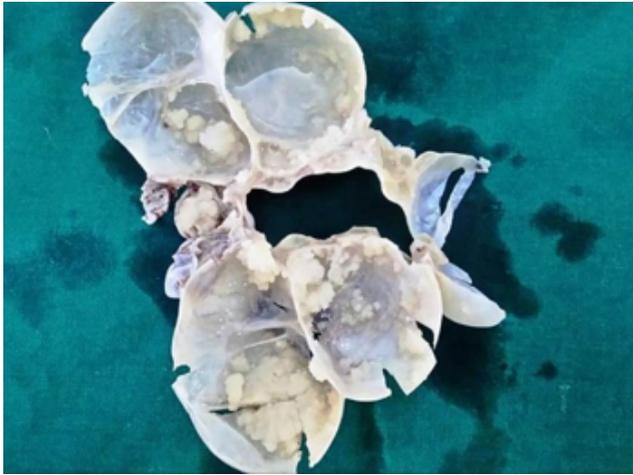


Fig. 1: Gross photograph of borderline serous tumor showing solid cystic lesion with papillary excrescences

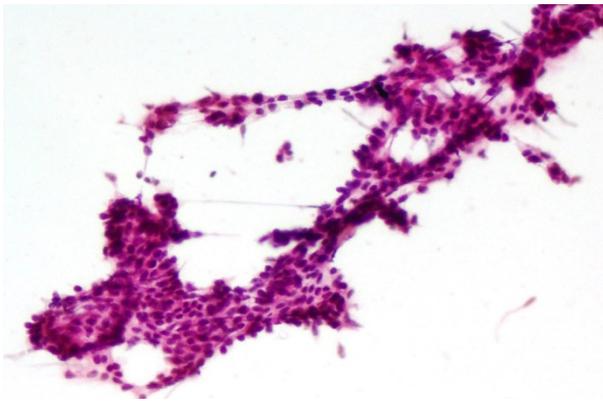


Fig. 2: Microphotograph shows cells arranged in a branching pattern in a serous cystadenoma. [H&Ex100]

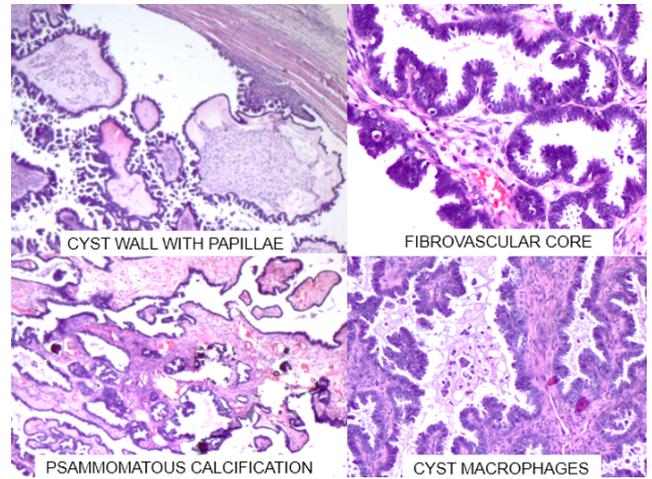


Fig. 3: Histopathological features of serous cystadenoma of the ovary showing cyst wall with papillae, fibrovascular cores, psammomatous calcification and cyst macrophages [H&Ex40]

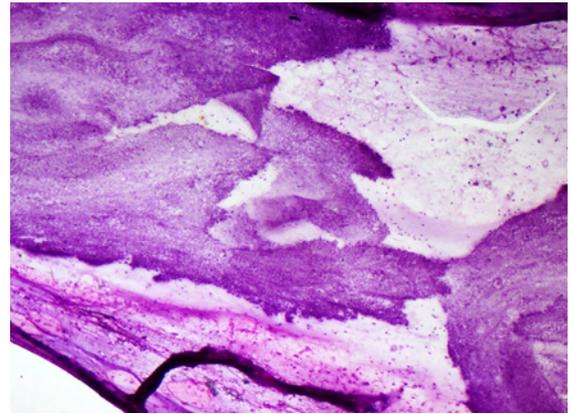


Fig. 4: Cytology of Mucinous cystadenoma with irregularly branching sheets of cells [H&E x40]

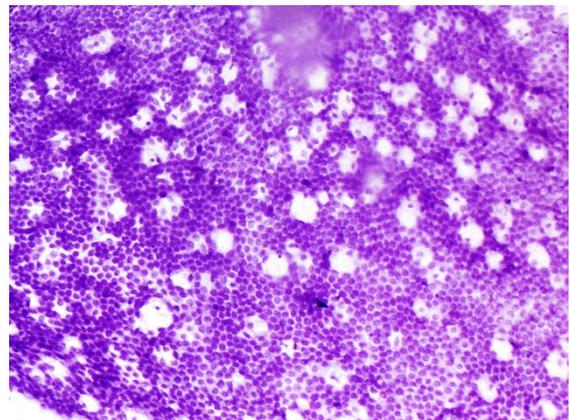


Fig. 5: Cytology of mucinous cystadenoma with sheets of cells with interspersed goblet cells [H&Ex200]

Table 5: Cytological features of epithelial ovarian neoplasms

Histological type of ovarian tumor	Cytological features
Serous tumors	<p>Benign serous tumors: Low cellularity, Papillary arrangement, small clusters or honeycomb sheets of benign, small round to cuboidal epithelial cells, Cytoplasm is scant and pale; nuclei are uniform and round with pale chromatin.[Figure 1, 2, 3]</p> <p>Serous borderline tumor : Papillary clusters, small clusters and monlayered sheets with few single neoplastic cells, the lesser degree of pleomorphism, and the less conspicuous nucleoli.</p> <p>Serous cystadenocarcinoma: Papillary groups with hyperchromatic nuclei and irregular coarsely granular chromatin. Occasional psammoma bodies may be seen.</p>
Mucinous tumors	<p>Mucinous cystadenoma: Columnar cells with basally placed nuclei and vacuolated cytoplasm, honey comb clusters in a mucinous background. [Figure1,2]</p> <p>Mucinous borderline tumors: Sheet-like groups or papillary configurations, overlapping cell clusters. Mildly atypical nuclei which may contain nucleoli, and cytoplasm with vacuoles of different sizes,</p> <p>Mucinous cystadenocarcinoma: Clusters and monolayered sheets, single cells with pleomorphic nuclei and vacuolated cytoplasm with background mucin. Severe nuclear atypia, overlapping tumor cell clusters and tumor diathesis</p>
Endometrioid tumors	<p>Endometrioid carcinoma: Nests of squamous cells mingled with sheets and overlapping clusters of small epithelial cells with hyperchromatic nuclei and scanty cytoplasm.</p>
Clear cell tumors	<p>Clear cell cystadenoma: Clear cells in papillary, gland like and sheets with bland nuclei and clear to eosinophilic cytoplasm.</p> <p>Clear cell borderline tumors: Presence of nuclear crowding, overlapping, occasional mitosis and mild nuclear atypia.</p> <p>Clear cell carcinoma: Clear cells in papillary, gland like and sheets Pleomorphic nuclei, moderate to abundant clear cytoplasm, few showing fine granulations; giant and multinucleate tumour cells Cluster of tumour cells with eosinophilic, hyaline, globular substance in the centre (Raspberry body or mirror ball pattern) Intracytoplasmic eosinophilic inclusions may also be seen</p>
Brenner tumors	<p>Benign brenner tumor: Sheets, small and large clusters of benign epithelial cells with ovoid grooved nuclei referred to as 'coffee-bean' nuclei intermingled with the deep orangeophilic keratinized squamoid cells.[Figure6,7] Abundant naked nuclei in the background, lack of nuclear pleomorphism and mitoses Fused and multilobated extracellular metachromatic hyaline globules.</p> <p>Borderline brenner tumor: Presence of nuclear pleomorphism, mitoses, and irregular nuclear membranes</p> <p>Malignant Brenner tumor : Clusters of polygonal cells or single cells with pleomorphic nuclei, granular chromatin and scant cytoplasm; Multinucleate cells may be seen.</p>

Table 6: Cytological features of sex cord stromal and germ cell tumors of ovary

Teratomas	<p>Mature cystic teratomas show anucleate and nucleate squamous cells, benign columnar cells, and a few neutrophils, lymphocytes, and macrophages in a background of thick amorphous material.</p> <p>Immature teratomas show neuroendocrine features, immature glial-like cells, neuroectodermal rosettes, squamous cells, and ciliated epithelium.</p>
Dysgerminoma	<p>Cohesive clusters of round to oval tumor cells with round to oval vesicular nucleus, prominent nucleoli and vacuolated cytoplasm admixed with lymphocytes in a tigroid background.[Figure 8,9]</p>
Yolk sac tumor	<p>Cellular smears with, tumor cells arranged in papillary groups, tight cell clusters and acinar pattern. Cells show enlarged, moderately pleomorphic, hyperchromatic nuclei and moderate amount of cytoplasm, some of which show vacuolation, displacing the nuclei eccentrically.</p>
Granulosa cell tumors	<p>Three-dimensional clusters, Rosettes, loosely cohesive syncytial aggregation and individual cells; nuclear grooves may be present, vacuolated cytoplasm. Call-Exner bodies. Exuberant capillaries associated with papillary like fronds (pseudopapillae) Theca cells are elongated, with hyperchromatic nuclei, indistinct nucleoli and blunt ends.</p>
Fibroma & Fibrothecoma	<p>Fibroma: Spindle cells similar to leiomyoma, low grade bland cytology Increase mitosis and atypia may be seen in cellular fibromas / fibrosarcomas</p> <p>Thecoma: Cells are plump, have irregular nuclei and fragile cytoplasm. Air dried smears show intracytoplasmic fat when stained with Oil red O.</p>

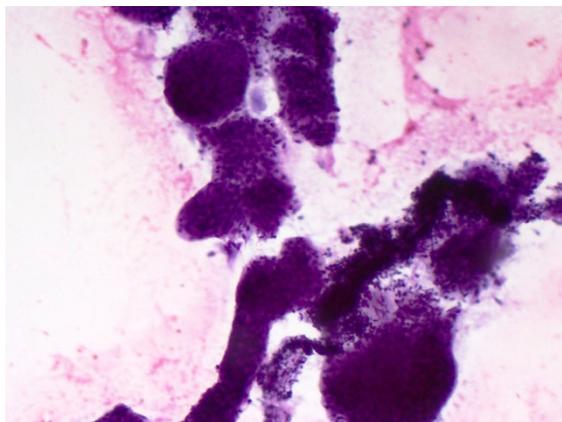


Fig. 6: Cytology of benign Brenner tumor with rounded three dimensional clusters of cells [H&E x40]

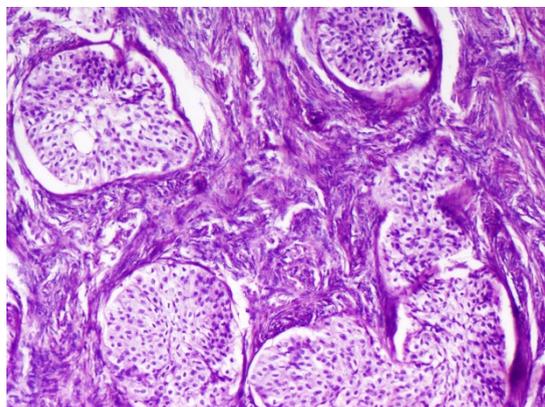


Fig. 7: Histopathology of Brenner tumor with nests of cells resembling the urothelium [H&Ex100]



Fig. 8: Gross photograph of dysgerminoma with lobulated, fleshy, solid tumor with uniform tan brown areas on cut section.

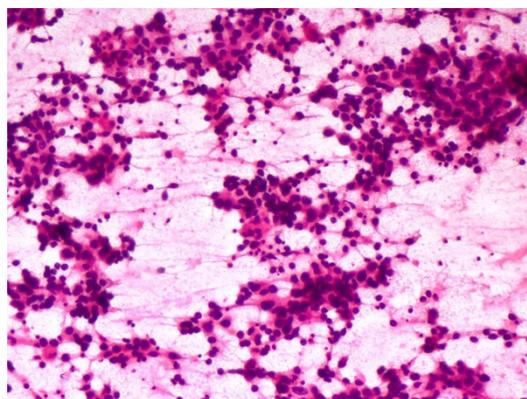


Fig. 9: Dysgerminoma on imprint cytology showing clusters and singly dispersed cells with sprinkling of lymphocytes. [H&Ex40]

Often ovarian malignancy is diagnosed at an advanced stage owing to a number of reasons. The anatomical problem being one of them. The ovaries are a tiny pair of organs, suspended on either side of the uterus. Unless significantly enlarged, they are not easily accessible by pelvic examination. Hence majority of cases present at an advanced stage with a poor 5-year survival rate. Thus accurate diagnosis is important for immediate treatment and management.^{2,3,8,10,15}

The accuracy of aspiration cytology diagnosis in patients with ovarian enlargement or cancer was reported by Vijaykumar A,¹ Melies M et al² and Sireesha A et al.³ In these reports, ovarian cancer was accurately identified in approximately 85-95% cases.

A careful gross examination is also very important and may be as accurate as frozen section and often avoid delays in diagnosis. Diagnosis of borderline tumors on imprint cytology is challenging. The pitfall includes remarkable heterogeneity of tumor from area to area within the same ovarian mass and sampling error.^{6,7} With respect to mucinous tumors, focal mild atypia can lead to a false positive diagnosis of mucinous borderline tumor. Therefore mucinous borderline tumors should have a significant proportion of cells showing nuclear atypia and overcrowding.^{14,15} A few authors have also stated the issue of technical factors and quality of frozen sections to influence the diagnosis. A confirmatory diagnosis of borderline neoplasia would require a less extensive surgical procedure, especially in younger patients who wish to retain fertility.^{10,12}

5. Conclusion

Intraoperative imprint cytology & frozen section are of immense value in diagnosis of ovarian tumors especially in guiding the surgeon within a short period of time. Knowledge of specific cytological features for each tumor type helps in accurate diagnosis which in turn is valuable

Table 7: Comparison of various studies with the present study

Type of ovarian neoplasm	Present study	Vijayakumar A ¹	Melies M, et al ²	Sireesha A et al ³
Surface epithelial tumors				
Serous tumors				
Benign serous cystadenoma	15	3	15	14
Borderline serous tumors	2	-	10	7
Serous cystadenocarcinoma	3	13	17	8
Mucinous tumors				
Mucinous cystadenoma	15	-	6	6
Borderline mucinous tumor	5	4	4	2
Mucinous cystadenocarcinoma	-	5	8	-
Endometrioid tumors:				
Benign cystadenoma	1	-	-	1
Endometrioid carcinoma)	2	2	4	-
Clear cell tumors:				
Clear cell adenocarcinoma	1	-	2	-
Transitional cell tumors:				
Brenner tumor -Benign	1	-	4	-
Sex cord-stromal tumors				
Fibromas	1	-	4	-
Fibrothecomas	1	4	6	-
Sclerosing sex cord stromal tumor	-	-	1	-
Sertoli -Leydig cell tumor				
Granulosa cell tumor	-	5	8	-
Germ cell tumors				
Mature cystic teratoma	2	8	8	-
Immature teratoma	-	-	1	-
Dysgerminoma	2	3	-	2
Mixed germ cell tumor	1	1	-	-
Metastatic adenocarcinoma				
Malignant mixed mullerian tumor	-	-	1	-
Total no of cases	53	50	100	40

Table 8: Comparison of sensitivity and specificity with other studies

Author	Sensitivity	Specificity
Stewart et al ¹²	93%	100%
Shahid et al ¹¹	95.8%	96%
Tushar et al ⁴	93%	92%
Present study	93.75%	97%

in immediate appropriate treatment and management of patients with benign or malignant neoplasms.

6. Source of Funding

None.

7. Conflict of Interest

The authors declare that there is no conflict of interest.

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Author biography

Archana Shivamurthy, Senior Resident

Padmapriya Jaiprakash, Associate Professor

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