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ORIGINAL ARTICLE

THE DIAGNOSTIC ACCURACY OF INTRA-OPERATIVE IMPRINT CYTOLOGY IN OVARIAN TUMORS

Chandrashekhar T[1], Govindraja E[2], Chandana N[3]

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ABSTRACT: OBJECTIVES: To establish the validity and reliability of imprint cytology and its accuracy in intra operative diagnosis of ovarian tumours and to compare it with the histopathology reports. **METHODS:** Multiple imprints were taken from 30 surgical specimens of patients suspected of ovarian neoplasms who underwent surgery as primary line therapy at our institution. This was compared with Final pathological diagnoses. We calculated the limits among benign, borderline, and malignant lesions, and analyzed the diagnostic accuracy. **RESULTS:** 30 cases were studied during this study period from November 2011 to October 2013. 19 (63.3%) cases were benign, 8 cases were malignant (26.7%), 1 (3.3%) case was borderline malignancy and 2 (6.7%) cases were excluded. Overall diagnostic accuracy was 96.4%. **CONCLUSION:** Imprint cytology is a less expensive, simple and quick method of diagnosis, and is reliable in terms of accuracy to aid decision making intraoperatively.

KEYWORDS: Ovarian tumors, imprint cytology, histopathological examinations, cytological and histopathological correlation of ovarian tumors.

INTRODUCTION: The ovarian tumors manifest with wide spectrum of clinical, morphological and histological features. Screening for ovarian epithelial cancer are improved by various diagnostic modalities, Doppler color flow ultrasonography and transvaginal ultrasonography, measurement of tumor markers such as Serum HCG, serum CA125, serum alpha – fetoprotein placental alkaline phosphatase and lactate dehydrogenase ovarian cancer antigen OVX 1 and CA15-3 and numerous, but their accessibility to the practicing gynecologist for rural based poor population remains very limited even today.[1]

Despite these, however it may not be possible to determine before surgery whether patients presenting with ovarian or adnexal masses have benign or malignant disease. Clinical, serological, and radiological findings are not completely specific and even the gross intra operative findings may be misleading.[2,3]

Assessing the nature of tumors confined to the ovaries is problematic because benign and malignant neoplasm can have identical gross appearances.[4,5]

As the optimal management of benign, borderline, and malignant ovarian tumors differs, especially in patients who wish to retain fertility, intra-operative assessment frequently is used to provide a provisional pathological diagnosis and to guide the extent of surgery and/or the requirement for additional staging procedures.[6,7]

Imprint cytology gives intraoperative diagnosis of ovarian tumors within 20 minutes. It is helpful especially in young patients who need conservative surgery in order to preserve fertility. It does not alter the quality of the biopsy specimen 13. Imprint cytology is a less expensive, simple and quick method of diagnosis, and is reliable in terms of accuracy.

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We under took this study to find out the accuracy of imprint cytology in intraoperative ovarian tumor diagnosis by correlating it with histopathology which is taken as the gold standard in diagnosis of ovarian tumors.

METHODS: In this prospective study all patients undergoing surgery for ovarian tumors from the period November 2011 to October 2013 were included. Patients who had taken radiotherapy, suspicious inflammatory ovarian masses, were excluded. Detailed clinical history, physical examination and investigations were recorded. Intra-operatively multiple imprint smears were taken from resected tumor masses, and stained with hematoxylin and eosin. Imprint cytology report were received within 20 min of smear preparation. Further lines of management were decided on table based on the imprint cytology report. After completion of the surgery, the resected masses were sent for histopathological study. Results of imprint cytology and histopathology were compared and diagnostic accuracy of intra-operative imprint cytology evaluated.

RESULTS: Out of 30 cases studied, 8 were diagnosed as malignant ovarian tumor, 17 as benign and 3 as borderline. 2 cases were abandoned, 1 was a case of CA-pancreas with metastasis and another was suspected case of GIST.

On imprint cytology examination, 17 cases were benign (56.7%), 8 cases were diagnosed to be malignant (26.7%) and 3 cases were borderline. Of the 17 benign lesions, 5 cases were serous cyst adenoma (16.67%), 8 cases of mucinous cyst adenoma (26.67%), 3 cases of simple benign cyst (10%), 1 case of fibroma were noted (3.33%). 3 cases (10%) of borderline mucinous cyst adenoma were noted.

Of the 8 malignant tumors, 3 were diagnosed as serous cyst adenocarcinoma (10%), 1 case of mucinous cyst adenocarcinoma (3.33%), other one was metastatic (Signet Ring cell type) adenocarcinoma (3.33%), 1 case of dysgerminoma (3.33%), 1 case of yolk sac tumor (3.33%) and one case of mixed germ cell tumor were noted (3.33%).

The 17 cases reported as benign as per imprint cytology report were not subjected for staging laparotomy and underwent conservative surgery in the form of cystectomy. The 3 patients who were diagnosed as borderline underwent staging procedure. The malignant tumor patients were subjected to optimal cyto reduction and staging.

Distribution of Ovarian tumors based on Imprint Cytology Report

Imprint cytology	Frequency	Percentage
Malignant	08	26.7%
Benign	17	56.7%
Borderline	03	10.0%
Non-ovarian tumors	02	06.7%
Total	**30**	**100%**

Table 1: Distribution based on Imprint cytology report

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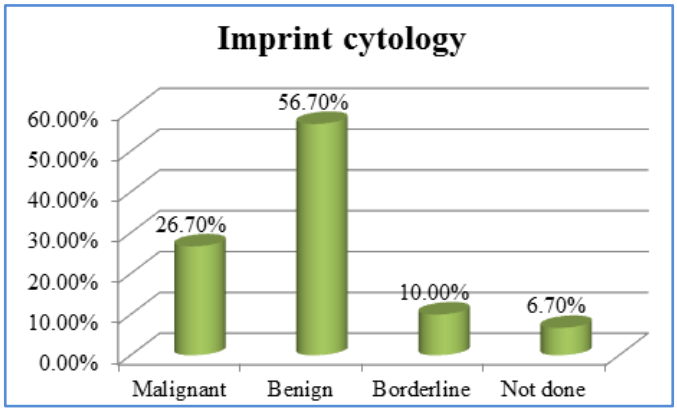

Graph 1: Distribution of Ovarian Tumours based on Imprint Cytology Report

	Imprint Cytology	Percentage
Epithelial tumors		
Serous		
Benign	5	16.67
Borderline	0	0.00
Malignant	3	10.00
Mucinous		
Benign	8	26.67
Borderline	3	10.00
Malignant	1	3.33
Endometrioid		
Benign	0	0.00
Malignant	0	0.00
Germ cell tumor		
Yolk sac tumor	1	3.33
Mixed Germ Cell Tumor	1	3.33
Mature cystic teratoma	0	0.00
Dysgerminoma	1	3.33
Sex cord stromal tumor		
Fibroma	1	3.33
Metastatic adenocarcinoma	1	3.33
Benign Cyst	3	10.00
Mixed Serous Mucinous Cystadenoma	0	0.00
No evidence of tumor	0	0.00

Table 2: Distribution of Ovarian Tumors based on Imprint Cytology Report

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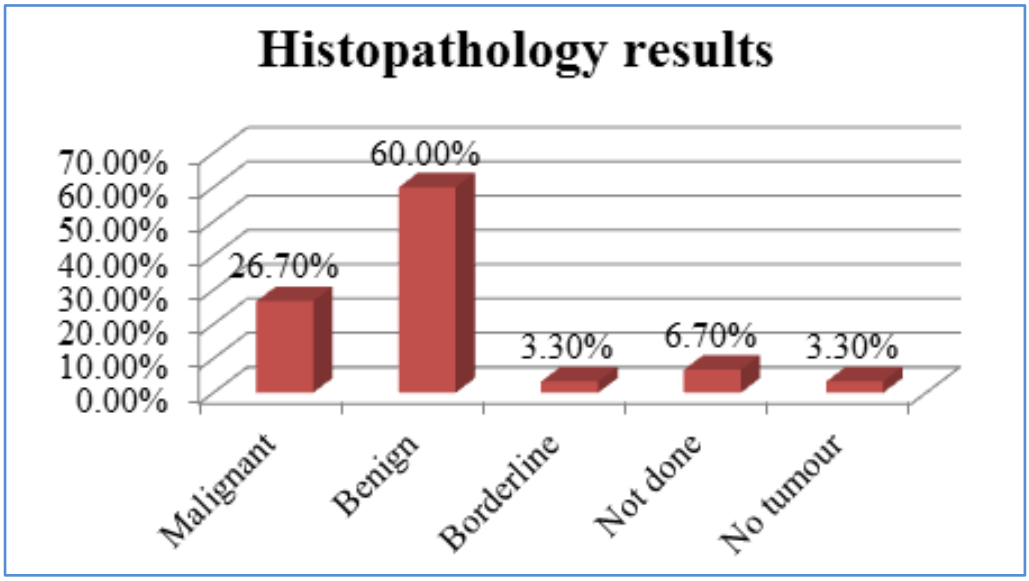
DISTRIBUTION OF OVARIAN TUMOURS BASED ON HPE: Of the 30 cases 8 cases were diagnosed as malignant, 18 were benign, 1 borderline and in 1 case no evidence of tumor was found. Out of the 18 benign cases 6 were serous cyst adenoma (20%), 7 were diagnosed as mucinous cyst adenoma (23.33%), 1 case as fibroma (3.33%), 3 cases as benign cyst (10%).

One case (3.33%) of borderline cyst adenoma was noted. One case (3.33%) of mixed serous-mucinous cyst adenoma was noted. Three cases (10%) of papillary serous cyst adenocarcinoma, one case (3.33%) of mucinous cyst adenocarcinoma, one case (3.33%) of malignant metastatic epithelial lesion (Signet Ring cell type) were noted.

3 germ cell tumors (10%) were noted, 1 yolk sak tumor (3.33%), 1 case (3.33%) of mixed germ cell tumor and one case (3.33%) of dysgerminoma were noted.

Histopathology report	Frequency	Percentage
Malignant	08	26.7%
Benign	18	60.0%
Borderline	01	03.3%
Not done	02	06.7%
No. tumor	01	03.3%
Total	**30**	**100%**

Table 3: Distribution based on histopathology report



Graph 2: Distribution based on HPE

On histopathological examination, 8 lesions were malignant, 18 were benign and 1 was borderline.

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	Histopathology Report	Percentage
Epithelial tumors		
Serous		
Benign	6	20
Borderline	0	0.00
Malignant	3	10.00
Mucinous		0.00
Benign	7	23.33
Borderline	1	3.33
Malignant	1	3.33
Endometrioid		0.00
Benign	0	0.00
Malignant	0	0.00
Germ cell tumor		0.00
Yolk sac tumor	1	3.33
Mature cystic teratoma	0	0.00
Dysgerminoma	1	3.33
Mixed Germ cell tumor	1	3.33
Sex cord stromal tumor		0.00
Fibroma	1	3.33
Metastatic adenocarcinoma	1	3.33
Benign Cyst	3	10.00
Mixed Serous Mucinous Cyst adenoma	1	3.33
No. evidence of tumor	1	3.33

Table 4: Distribution based on Histopathological Report

Comparison of Imprint cytology and histopathology report.

Nature of lesion	Imprint cytology	Histopathology report
Malignant	08 (28.6%)	08 (28.6%)
Benign	17 (60.7%)	18 (64.2%)
Borderline	03(10.7%)	01 (03.6%)
No. Tumor	--	01 (03.6%)
Total	**28 (100%)**	**28 (100%)**

Table 5: Comparison of Imprint cytology and histopathology report

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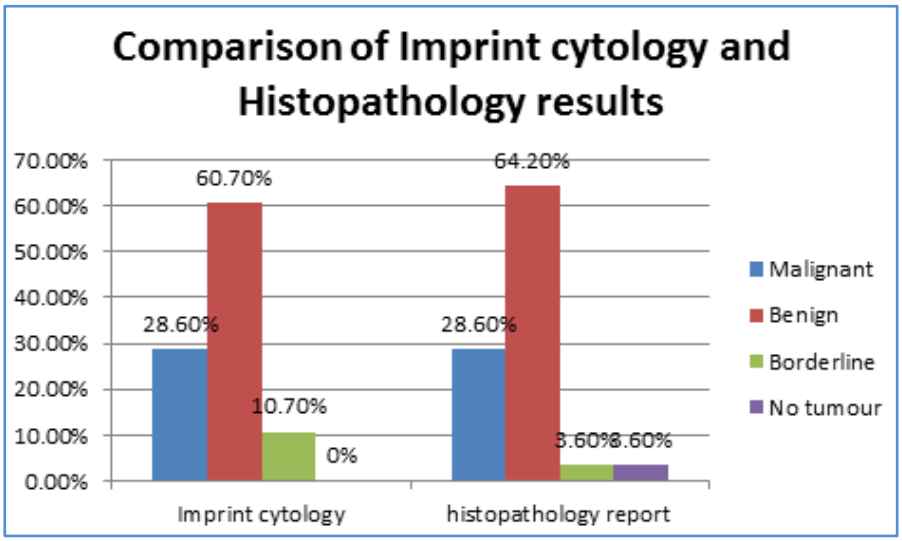

Graph 3: Comparison of Imprint Cytology and histopathology results

	Imprint Report	Percentage	Histopathology Report	Percentage
Epithelial tumors				
Serous				
Benign	5	16.67	6	20
Borderline	0	0.00	0	0.00
Malignant	3	10.00	3	10.00
Mucinous				0.00
Benign	8	26.67	7	23.33
Borderline	3	10.00	1	3.33
Malignant	1	3.33	1	3.33
Endometrioid				0.00
Benign	0	0.00	0	0.00
Malignant	0	0.00	0	0.00
Germ cell tumor				0.00
Yolk sac tumor	1	3.33	1	3.33
Mature cystic teratoma	1	3.33	0	0.00
Dysgerminoma	1	3.33	1	3.33
Mixed Germ Cell	0	0.00	1	3.33

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Sex cord stromal tumor				
Fibroma	1	3.33	1	3.33
Metastatic adenocarcinoma	1	3.33	1	3.33
Benign Cyst	3	10.00	3	10.00
Mixed Serous Mucinous Cystadenoma	0	0.00	1	3.33
No. evidence of tumor	0	0.00	1	3.33

Table 6: Comparison of Imprint Cytology and Histopathological results

Imprint cytology	Frequency	Percentage
Correct correlation with HPE	25	89.3%
Not correct with HPE	03	10.7%
Total	**28**	**100%**

Table 7: Validity of Imprint cytology report

Of the 28 cases that were submitted for intraoperative imprint cytology, 25 cases correlated (89.3%) and 3 cases (10.7%) did not correlate. The 3 cases were discordant. Out of these one was a case of mucinous cystadenoma which was reported as serous cyst adenoma, one case reported as borderline epithelial tumour did not show any evidence of malignancy on histopathology. One case which was diagnosed as borderline was reported as benign by histopathological examination.

For malignant ovarian tumors the cytology was 100% concordant with histology. Total of 8 (28.6%) malignant tumors were reported. The overall accuracy for diagnosing malignancy by cytology is 100%.

3 (10.7%) cases of borderline tumors were reported as per cytology out of which only one (3.6%) case was concordant. One case showed no evidence of tumor. Another case was diagnosed to be benign epithelial tumor. Accuracy for diagnosing a borderline ovarian tumor by imprint cytology is 66.7%

Total of 17 (60.7%) cases were reported as benign ovarian tumor as per cytology and all the 17 cases correlated with histopathology.

Accuracy for diagnosing benign ovarian tumors by imprint cytology is 90.9%.

Overall accuracy for diagnosing ovarian tumors in comparison with histopathology is 96.4%

DISCUSSION: A total of 30 cases were studied, out of which 18 (60%) were benign, 8 (26.7%) were malignant, 1 (3.3%) was of borderline malignancy. A study by Pilli et al[8] also showed 75.2% benign, 2.8% borderline and 21.9% malignant lesions which was in concordance with our study.

Histologically total 30 patients who presented with ovarian tumors were studied. The tumors were classified according to WHO classification. Surface epithelial tumors were the commonest variety constituting 60.7% of all the ovarian tumors followed by germ cell tumors 28.1%, sex cord

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stromal tumors 10.1%, and metastatic tumors 1.1%. The comparative analysis of study with other authors like Pilli et al[8] and Jha R[11] and Karki S[9] showed the following data.

Surface epithelial tumors are the most common ovarian tumors encountered accounting for 79.17% of cases in the present study. The incidence is comparable with other studies, 71% in Pille et al, 79% in Jha R and Karki S and 52.2% in Yasmin et al.

Germ cell tumors are accounted for 12.5% cases in the present study. Pille et al reported an incidence of 7%, Jha R and Karki S 1.5% and Yasmin et al 42.2%. Incidence of Sex-cord tumors are accounted for 4.17% cases in the present study. Pille et al reported an incidence of 21%, Jha R and Karki S 16% and Yasmin et al 3.1%. Metastatic tumors accounted for 4.17% cases in the present study. Pille et al reported an incidence of 0.7%, Jha R and Karki S 12% and Yasmin et al 2.4%.

Incidence of benign lesions are accounted for 60.7% cases in the present study. Kar Tushar et al reported an incidence of 53.77%, Suen KC et al 70.18% and Colin 59.4%. Incidence of borderline lesions accounted for 10.7% cases in the present study. Kar Tushar et al reported an incidence of 7.5%, Suen KC et al 5.26% and Colin 6.05%. Incidence of malignant lesions accounted for 28.6% cases in the present study. Kar Tushar et al reported an incidence of 38.8%, Suen KC et al 24.56% and Colin 34.4%.

Incidence of benign lesions are accounted for 64.2% cases in the present study. Kar Tushar et al reported an incidence of 53.7%, Suen KC et al 66.67% and Colin 56.21%. Incidence of borderline lesions accounted for 28.6% cases in the present study. Kar Tushar et al reported an incidence of 7.5%, and Colin 8.7%. Incidence of malignant lesions accounted for 3.6% cases in the present study. Kar Tushar et al reported an incidence of 38.8%, Suen KC et al 21% and Colin 35.07%.

The overall diagnostic accuracy of imprint cytology in comparison with histopathology in our study was 96.4% and was comparable with other studies which was 89.55 in Kar Tushar et al[10], 93.8% in Suen KC et al[2] and 97.8% in Colin[3]

CONCLUSION: We undertook the study for the comparison of imprint cytology and histopathological analysis of various patterns of ovarian tumors for a period of two years. A total of 30 cases were studied. Imprint cytology was used intraoperatively to provide diagnosis regarding the type of lesion and further decisions about the extent of surgery was based on the imprint cytology report.

The imprint cytology is a simple and rapid diagnostic technique, which does not require any sophisticated equipment. Considering its high accuracy it may be routinely used as an adjunct to frozen section especially when cryostat machines or microwave tissue processors are not available for rapid diagnosis.

Since imprint of freshly resected specimen yields smears with excellent cytological clarity owing to the single cell thickness that the smears offer, it still holds a unique status even in the current perspective. Hence, imprint cytology is worthy of being recommended as an imperative procedure for rapid intra-operative evaluation of the type of lesion and for making decisions regarding extent of surgery and management thereafter.

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Figure 1: Bilateral serous cyst adenocarcinoma (intraoperative): external surface is bossellated with congested vessels. Cut section shows solid cystic areas with soft papillary excrescences and focal areas of necrosis

Fig. 1

Figure 2: Serous cyst adenocarcinoma: Imprint shows scattered clusters of epithelial cells with high N: C ratio, prominent nucleoli, in a hemorrhagic back ground, H&E 200x (inset): complete papillary frond , H&E 40x.

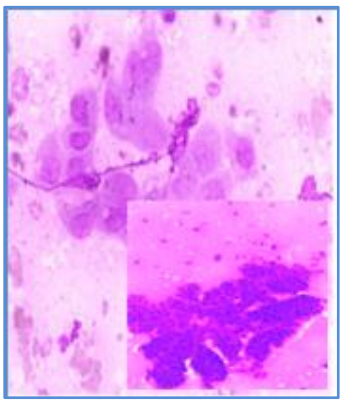

Fig. 2

Figure 3: Serous cyst adenocarcinoma (HPE): tumor has closely packed papillae, lined by pleomorphic cells with overlapping irregular nuclei with fine chromatin & prominent nucleoli H&E, 200x. Inset: shows papillary fronds with fibrous cores. H & E 40x.

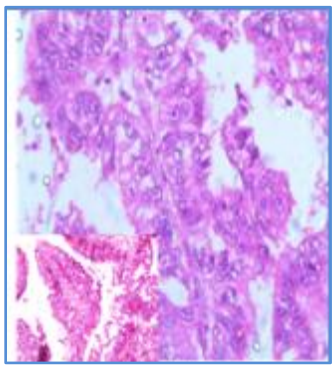

Fig. 3

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Figure 4: Mucinous Cyst adenoma (HPE): shows cyst wall lined with columnar cells in a single row with no nuclear atypia, H&E, 40X.

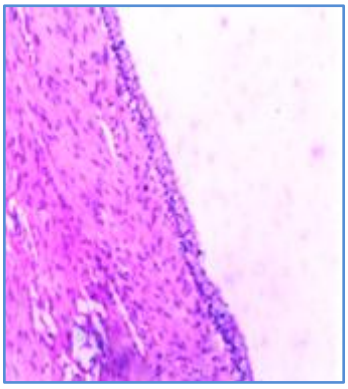

Fig. 4

Figure 5: Mucinous cyst adenoma: Imprint shows monolayered sheets of tumor cells with vacuolated cytoplasm. Toluidine blue 40X (inset): honey comb pattern with distinct cell borders H&E 100X.

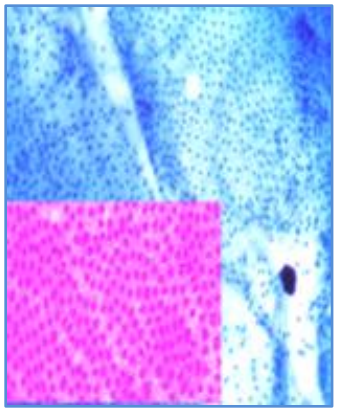

Fig. 5

Figure 6: Borderline mucinous cyst adenoma: Imprint shows cohesive clusters of cells with moderate increase in N/C ratio and coarse chromatin H&E100x.

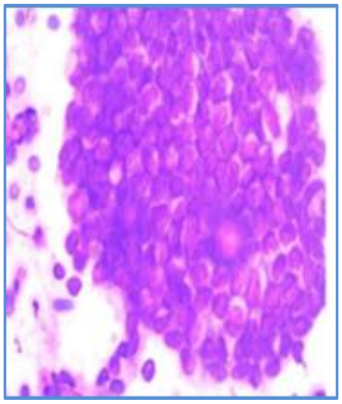

Fig. 6

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Figure 7: Borderline mucinous cyst adenoma: shows multilayered cells with moderate increase in N/C ratio. H & E 40x.

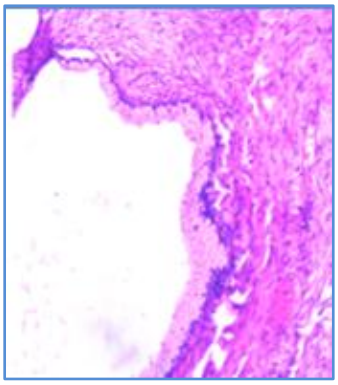

Fig. 7

Figure 8: Metastatic Signet ring cell carcinoma: HPE shows normal ovarian follicular lining with abundant signet ring cells infiltrating the stroma.H&E40x.(inset)variable sixed signet ring cells with single large vacuole pushing nucleus to periphery H&E 400x.

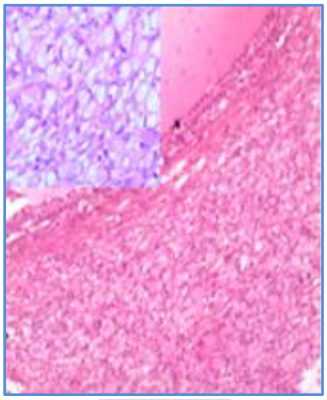

Fig. 8

Figure 9: Metastatic Signet ring cell carcinoma: imprint shows highly cellular smears composed of signet ring cells H &E 200x.

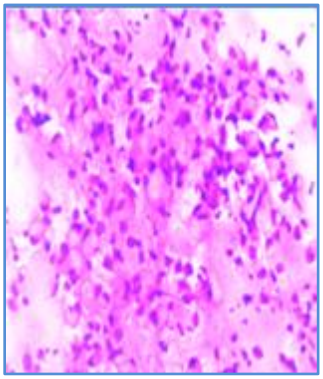

Fig. 9

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AUTHORS:

1. Chandrashekhar T.
2. Govindraja E.
3. Chandana N.

PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of Obstetrics and Gynaecology, Vijayanagara Institute of Medical Sciences, Bellary.
2. Professor, Department of Surgery, Vijayanagara Institute of Medical Sciences, Bellary.
3. Junior Resident, Department of Obstetrics and Gynecology, Vijayanagara Institute of Medical Sciences, Bellary.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Chandrashekhar T,
Room No. 4,
Department of Obstetrics and Gynecology,
Vijayanagara Institute of Medical Sciences,
Bellary.
Email: cstobg@gmail.com
aralichandan@gmail.com

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