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Usefulness of touch Imprint Cytology in Cancer diagnosis: A study of 119 cases

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Abstract

Touch imprint cytology is a valuable tool in surgical Oncology. It has been used in Neuropathology for many years and more recently it has been receiving increased attention in other areas of Pathology, like evaluation of sentinel lymph node biopsy, breast cancer, tumor margins, autopsy etc. As compared to Frozen Section, it is reliable and cost effective method, provides excellent cellular details. Examination of cytology specimens obtained by touch preparation of the fresh specimen can add a great deal of information to the frozen sections, and sometimes obviates the need for them altogether. Ability of TIC to identify malignancy with specific subtype is 86.31%. The positive predictive value was 100% and negative predictive value was 77% for the test. The simplicity, speed and cost effectiveness along with its ability to maximize cell recovery from very small tissue piece makes Touch Imprint Cytology a valuable resource for virtually every aspect of experimental and diagnostic medicine. TIC does have major limitations in differentiating invasive carcinoma from in-situ counterpart. Hence emphasizing the need of FS or HP examinations in cases where invasion is the sole criteria to define carcinoma.

Keywords: Touch imprint cytology, cancer diagnosis.

Introduction

In a landmark paper published in 1927, Dudgeon and Patrick first described the use of imprint smears of fresh tissues in the rapid microscopical diagnosis of tumors[1]. Touch imprint cytology is a valuable tool in Surgical Oncology. It has been used in Neuropathology for many years and more recently it has been receiving increased attention in other areas of Pathology[2]. like evaluation of sentinel lymph node biopsy[3], breast cancer[4], tumour margins[5], autopsy[6] etc. As compared to Frozen Section, it is reliable and cost effective method, provides excellent cellular details[7]. Examination of cytology specimens obtained by touch preparation of the fresh specimen can add a great deal of information to the frozen sections, and sometimes obviates the need for them altogether[8]. While diagnosing malignant tumour it is critical to obtain clear margins to minimize local recurrence. However, avoiding multiple re-excisions for margin clearance helps optimize cosmetic results in patients undergoing breast conservation surgery. Intra-operative touch preparation cytology (IOTPC) may decrease the need for multiple re-excisions and thereby improve cosmesis. The literature suggests that IOTPC can be useful in evaluation of margins[9]. Recently, Touch imprint cytology is also used as an adjunct to assess the adequacy of the sample obtained by Ultra Sound or CT guided biopsies and is found to be very useful in reducing the number of passes a radiologist mayhave to performon a particular patient[10-12]. The simplicity, speed and cost effectiveness along with its ability to maximize cell recovery from very small tissue piece makes Touch Imprint Cytology a valuable resource for virtually every aspect of experimental and diagnostic medicine[12]. In spite of its limitations like inability to differentiate in-situ carcinoma from invasive carcinoma and also inability to provide architectural details, Touch Imprint Cytology has got definite role in Intra Operative diagnosis that would guide the Surgeon's hand[2]. In an era in which cost-containment has become a critical factor we sought to investigate the diagnostic accuracy and usefulness of Touch Imprint Cytology in Cancer diagnosis[7].

Material and Methods

This was a cross sectional study, subjected to cytologic evaluation in addition to routine histology on Surgical Pathology samples suspected for neoplasia received at Surgical Pathology Section, Central Diagnostic Laboratory, Shree Krishna Hospital, Karamsad during the period of April 2009 to September 2010. Only fresh and unfixed tissues were included in the study. Normal tissue and inflammatory lesions were not included in the study. For each case, three consecutive smears were taken and were examined for cellularity, patterns, cytological features, background and concordance with histology. Clinically suspected malignancies which were later on found to be benign on histopathology were also included in this study. When stained, most of the smears on naked eye examination showed "IMPRINT" of tissue from which they were taken in a true sense. Imprints taken afterapplying gradual increasing pressure yielded smears with increasing darker stains, suggesting higher cellularity in successive smears.The prepared

smears were stained by Haematoxylin and Eosin, Papanicolaou Stain (Rapid –Pap) and Modified May – Grunewald's stain. While reporting the imprint cytology parameters like cellularity, patterns, cell morphology were evaluated in each case.
Concordances of Histo-Cytology for malignant tumorswere assessed by using a point system: 0 point - Slides of non-diagnostic quality; 1 point - Slides show either benign or atypical cells; 2 point - Slides with malignant cells present but in which a specific cell type cannot be recognized; 3 point - Slides revealing the specific malignant histologic cell type.

Concordances of Histo-Cytology for benign tumours were assessed by using following point system: 0 point - Slides of non-diagnostic quality; 1 point - Slides revealing a concordant diagnosis with Histology.

Results and Discussion

Total number of specimen evaluated during study period: 119. Of the total 119 specimens, 80% were diagnosed being malignant which is similar to study conducted by S.Sherley et al[7]. In her study malignant lesions were 75 %. They represented wide spectrum of tissues and lesions. In our study benign tumours and non-neoplastic lesions accounted for 20%. The study included 95 malignant lesions and 24 benign lesions.

Table-1
Overall smear cellularity (for both benign and malignant lesions)

Cellularity	Frequency	Percentage
Acellular	3.0	2.5
Scant	9.0	7.6
Moderate	25.0	21.0
High	82.0	68.9
Total	119.0	100.0

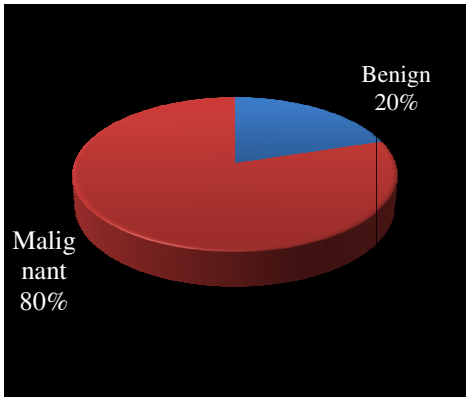

Figure-1
Distribution of Benign and Malignant lesions

In the present study male patients comprised of 40 % and females 60%. Male to female ratio was 0.66:1. The various cases were in the age group ranging from 3 years to 110 years, the mean age being 48.4 years (table-3).

Table-2
System/Organ wise distribution of specimens

Sr. No.	Organ	No. of cases	Percentage %
1	Breast	34	28.57
2	Lymphnode	38	31.93
3	Thyroid	8	5.04
4	Buccal mucosa	4	1.68
5	Parotid	2	5.88
6	Eye	2	1.68
7	Olfactory	2	0.84
8	CNS	4	6.72
9	Upper GI	3	0.84
10	Colo– rectal	6	0.84
11	Pancreatic	1	1.68
12	Testicular	2	3.36
13	Penis	2	0.84
14	Endometrium	1	1.68
15	Ovary	1	1.68
16	Cervix	2	1.68
17	Vulva	1	0.84
18	Kidney	1	0.84
19	Soft tissue	3	0.84
20	Bone	1	1.68
21	Skin	1	0.84
	Total	119	100.00

Table-3
Male : Female Ratio

Author	Year	Male	Female	Male : Female ratio
Peter F. Hahn et al	1995	50%	50%	1:1
Shirley S et al	2005	55%	45%	1.2:1
Present study	2010	40%	60%	0.66:1

The diagnosis on permanent paraffin histopathological sections was considered final against which the TIC diagnosis were compared for the accuracy. In our study depending on the cytomorphological features in the imprint smear,the lesions were grouped into four main categories.

0 Score: In these cases the slides were of non-diagnostic quality. There were three cases in this category in our study viz. NE carcinoma of breast, TCC of renal pelvis and a case of nodular sclerosis Hodgkin's lymphoma. There was no case in this category in study conducted by Hahn et al[13] and Ahmareen Khalid et al[14].

1 Score: In these cases smears showed either benign or atypical cells. There were four such cases in our study. The diagnosis of all four cases were deferred till permanent sections. These lesions were squamous cell carcinoma of buccal mucosa, squamous cell carcinoma of penis, adenocarcinoma of sigmoid

and a case IDC breast. There were 29.2% and 12% cases of this category in the study conducted by Hahn et al. and Ahmareen Khalid et al[14] respectively compared to 4% in the present study.

2 Score: In this category malignant cells were present in slides but a specific cell type could not be recognized. E.g. In a case of carcinoma of the esophagus with neuroendocrine differentiation, neuroendocrine component could not be appreciated. Hence, malignancy was made out from the smears but specific subtype was not identified. There were ten cases (11%) in this category in present study compared to 12.5% and 16.66% found by Hahn et al. and Ahmareen Khalid et al.[14] in their study.

3 Score: In these cases specific malignant histologic cell type was present in the smears. There were seventy eight cases (82%) in this category. Hahn et al. and Ahmareen Khalid et al found 58.3% and 71.66% cases respectively in this category.

Table-4
Accuracy Point distribution in malignant lesions

Accuracy Point	No. of cases	Percentage
0	3	3
1	4	4
2	10	11
3	78	82
Total	95	100.0

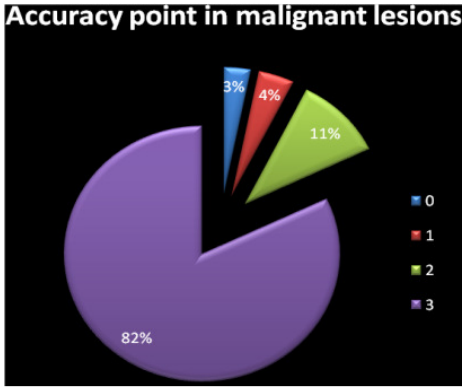

Figure-2
Accuracy Point distribution in malignant lesions

Table-5
Accuracy Point distribution in malignant lesions

Investigator	Year	Total no. of cases	Accuracy Point (%)			
			0	1	2	3
Hahn et al.	1995	24	0 (0)	7 (29.2)	3 (12.5)	14 (58.3)
Ahmareen Khalid et al.	2004	60	0 (0)	7 (12)	5 (8)	48 (80)
Present study	2010	95	3 (3)	4 (4)	10 (11)	78 (82)

Table-6
Average accuracy point

Investigator	Year of study	Average accuracy point
Hahn et al.	1995	2.1
Ahmareen Khalid et al.	2004	2.68
In present study	2010	2.71

In our study, the average accuracy point was 2.71. It is comparable with the studies conducted by Hahn et al. and Ahmareen Khalid et al[14] with average diagnostic accuracy point of 2.1and 2.68 respectively.

Table-7
Results

Investigator	Year	Accuracy	False positive
Mavec et al	1967	93%	-
Walker and Going	1976	95%	-
K. C. Suen et al	1978	98.3%	1.7%
S. Sherley et al	2005	92.2%	0%
In present study	2010	92.63%	0%

For malignant lesions, the overall accuracy for this method was 92.63 %, with a false-negative rate of 7.36 %. Ability of TIC to identify malignancy with specific subtype is 86.31%. S Ahmareen et al. in his study found it to be 96.6%.

For benign lesions, the overall accuracy for this method was 100%, with 0% false negative. The positive predictive value was 100% and negative predictive value was 77% for the test. The range for overall accuracy rate in literature varied from 66% to 100%. Our result is comparable with those of KC Suen et al[27] and S. Sherley[6] where the accuracy ranged from 92 to 98.3%.

No false positive case was identified in this study, suggests that a diagnosis of malignancy by the imprint method is highly reliable and specific and was comparable with the study conducted by S. Sherley at al.

When a lesion is grossly malignant, for example, most cases of mammary carcinoma and many cases of metastatic carcinoma in lymph node, especially when the primary cancer site is known, it is necessary only to confirm the gross impression. Imprints made from such cases, if clearly positive, would be sufficient for the purpose of intraoperative diagnosis. On the other hand, our 7.0% false-negative rate indicates that a negative imprint does not necessarily exclude malignancy. Imprints should always be interpreted in the light of gross findings; a negative diagnosis should be disregarded if the gross appearance of the lesion suggests malignancy.

Patterns: Imprint smears showed architectural patterns similar to their histopathological sections.

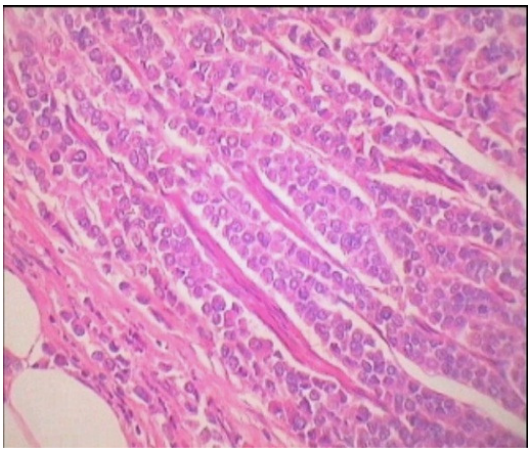
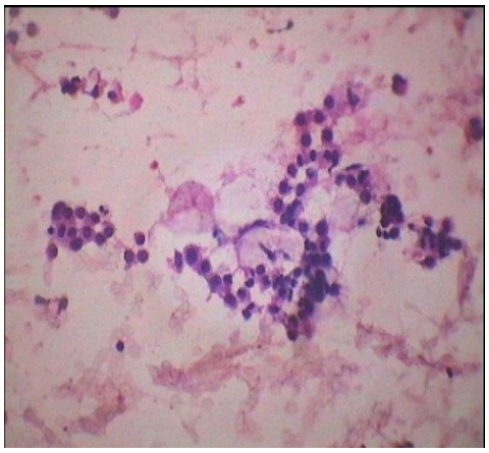

Figure-3
H.P. Infiltrating lobular carcinoma of the breast Classical Indian file pattern observed in TIC

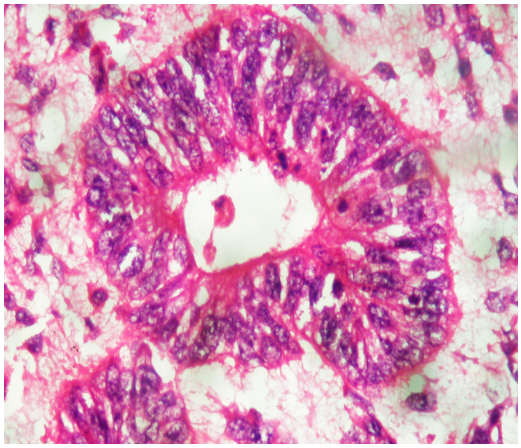
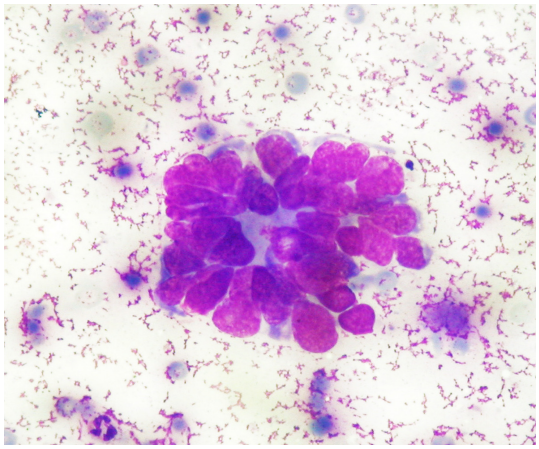

Figure-4
HP Mixed Germ cell tumourTIC of Germ cell tumour of testis

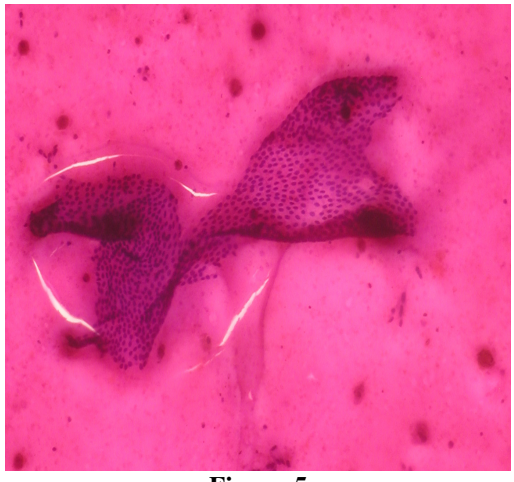

Figure-5
TIC of Adenomatous hyperplasia of thyroid

Large monolayeredsheet of benign follicular cell with good colloid.

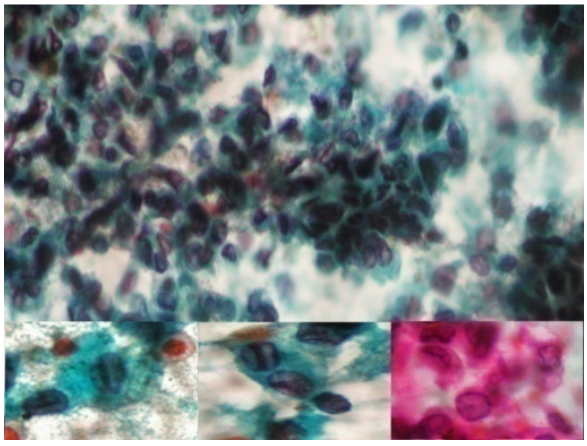

Figure-6
TIC of Papillary carcinoma of the thyroid

Papillary cluster of cells with first two inset pictures showing prominent nuclear grooves and the last showing nuclear clearing.

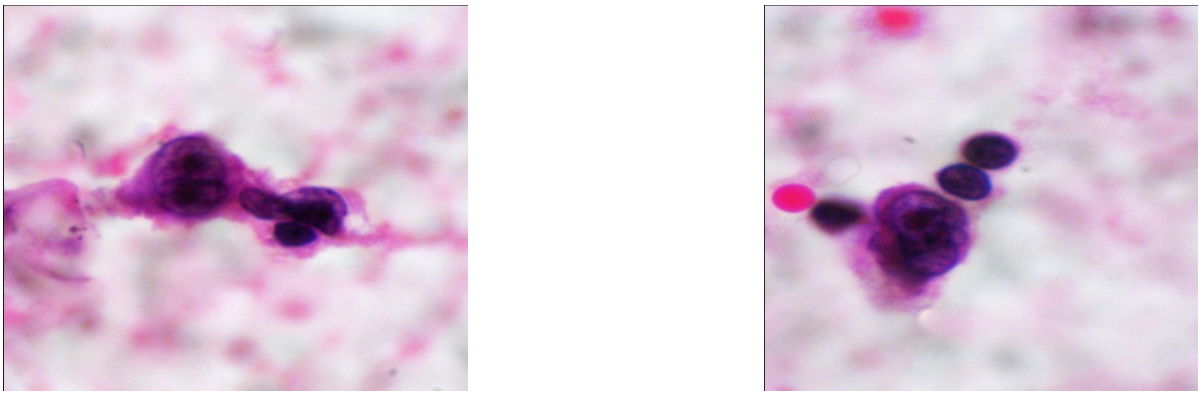

Figure-7
TIC of Hodgkin Lymphoma, NS- Classical Reed-Sternberg cells seen.

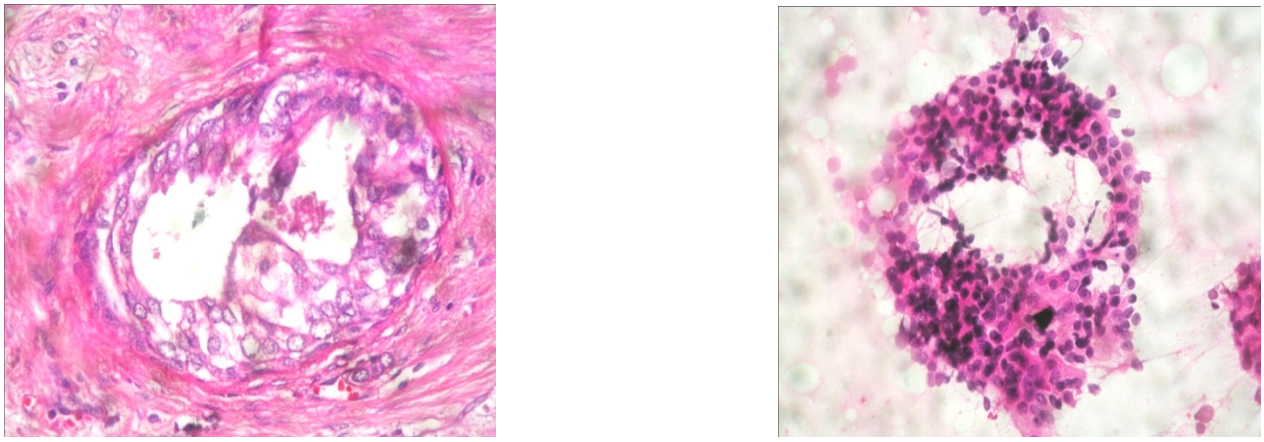

Figure-8
Histopathology of Neuroendocrine Carcinoma of Breast TIC of corresponding section

TIC provides crisper cytological details and fewer artefacts which was evident in cases of papillary carcinoma of thyroid, lymphomas and NE carcinoma of the breast. The touch preparations tended to contain much larger and more cohesive cell groups, revealing more architectural detail of tumor when present.

The usefulness of TIC is not limited to simple differentiation between benign and malignant lesions. It has been found quite reliable and useful in sentinel lymph nodes, gynaecological and thyroid malignancies. TIC has special role in brain and spinal cord lesions as these tissues are quite soft and was very useful in anaplastic astrocytoma, central neurocytoma and other lesion.In basal cell carcinomas and malignant melanoma of skin where a lot of frozen sections were needed to evaluate margins, TIC has provided satisfactory results without much pain and sweat. In spite of being inexpensive, simple and quicker than Frozen Section, TIC does have major limitations in differentiating invasive carcinoma from in-situ counterpart. Hence emphasizing the need of Frozen Section or HP examinations in cases where invasion is the sole criteria to define carcinoma.

Conclusion

The imprint smear technique is simple, rapid and does not require sophisticated instruments. The smears showed almost perfect concordance in majority of the neoplastic lesions and hence can be used routinely as an adjunct to histopathology. The method was useful in the rapid evaluation to identify the primary tumour and also for evaluation of draining lymphnodes. TIC has been found quite reliable and useful in determination of sentinel lymph nodes, gynaecological and thyroid malignancies. TIC has special role in brain and spinal cord lesions as these tissues are quite soft and was very useful in anaplastic astrocytoma, central neurocytoma and other lesions. TIC has further advantage of being inexpensive, simple and quicker than frozen section. A reference file of imprint slides with corresponding tissue sections maintained in the laboratory can provide very useful cytological information, aiding in histopathological examination and can become very useful teaching tool.

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